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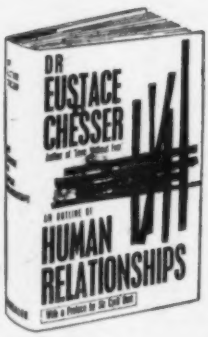

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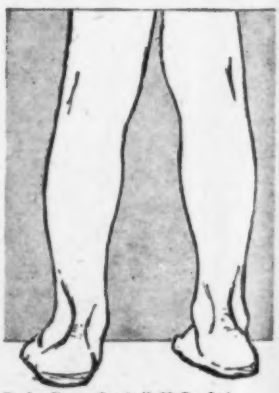

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A HOSPITAL STUDY OF CONGESTIVE HEART FAILURE, WITH SPECIAL REFERENCE TO COR PULMONALE

BY A GROUP OF PHYSICIANS* OF THE SHEFFIELD HOSPITAL REGION

Compiled by Professor C. H. STUART-HARRIS, with the assistance of Drs. R. S. H. TWIDLE and MARJORIE CLIFTON

Pulmonary heart failure, or cor pulmonale, is common in some parts of Britain, and Flint (1954) found that it accounted for a quarter of the cases of heart failure admitted to one Sheffield hospital (the City General Hospital). Yet, as was pointed out by Wood (1956), there are few comparative figures, and in the mortality statistics quoted by Southwood (1959) it receives scant mention. During 1954 to 1956 a study was made in hospitals of the Sheffield Hospital Region in order to compare the relative frequency of the various causes of heart failure in Sheffield and in other areas. A secondary purpose of the study was to compare the symptoms and signs, personal habits, occupation, and residence in the patients suffering from various forms of heart failure.

Method of Study

The hospitals chosen for the study were the City General Hospital in Sheffield and the general hospitals in Leicester, Nottingham, Derby, Scunthorpe, Mansfield, and Grimsby. In each hospital all patients with a diagnosis of congestive heart failure were examined as soon as possible after admission and admitted to the study, provided that they showed a raised jugular venous pressure and/or hepatomegaly and also oedema of the lower extremities and/or back. Patients aged 70 or over were excluded because of the difficulty of obtaining histories and personal data from them and because geriatric units were not included in the investigation. It was realized that the study would not provide evidence concerning the total prevalence of heart failure in any town or district, but this disadvantage was inevitable. A record card containing details of the patient (Fig. 1) was completed by a registrar or senior registrar as soon as possible after admission, but in each hospital the case was discussed with a consultant, who was responsible for the ultimate diagnosis and classification. Necropsies were performed whenever possible on those who died, and the records of the findings were completed on a standard form. The necropsy findings were taken into account in the final diagnostic classification, and batches of case records, together with *x*-ray films and electrocardiograms, were reviewed by the consultant in charge of the study in each area with one of the Sheffield workers.

This procedure was followed in order to standardize so far as possible the records of many different observers. Exact diagnostic criteria were not established at the outset, for the objective was that of assigning each case of congestive heart failure to one of a series of diagnostic groups based upon reasonable evidence of the causation of the heart failure. Thus the presence of valvular heart disease with a history either of rheumatic disease or characteristic valvular involvement led to the classification of the patient in the rheumatic group. Patients with hypertension were classified separately from those with evidence of ischaemic heart disease with or without myocardial infarction. As, however, there were many instances of hypertension with ischaemia, all patients with one or both of these conditions were later combined into a single degenerative group. When hypertension existed but the clinical picture was otherwise concordant with cor pulmonale, the patient was classified as a case of cor pulmonale. This was done whether or not the blood pressure returned to normal levels when the heart failure had subsided.

Cor pulmonale was diagnosed in patients with a history and signs of chronic chest disease provided that the clinical, radiological, and electrocardiographic findings were consistent with this diagnosis rather than with ischaemic heart disease. When the cause of heart failure was thought to be thyroid disease, or anaemia, or an acute infection of the lung without preceding chronic disease the case was placed in a "miscellaneous" category. Patients with congenital heart disease, pulmonary embolism leading to acute right heart failure, carcinoma, gross obesity, or without any discoverable cause for the failure were also placed in the miscellaneous group, largely because of the small numbers concerned.

Thus the final classification of each patient depended upon the clinical diagnosis supported by radiological and electrocardiographic evidence and, when available, by the necropsy findings. After conclusion of the assembly of the series, each record card was coded and the data were transferred to a punch-card. The latter cards were sorted in a Powers-Samas machine. The following analysis covers the complete series of patients from Sheffield and Derby, but only those studied during the first winter season in the other areas.

*The following participated in this study:— Sheffield (City General Hospital): Drs. F. J. Flint, J. P. Caley, and R. W. Meikle. Derby: Drs. E. J. S. Woolley and D. S. Harling. Leicester: Drs. S. E. Tanner, D. F. Lawson, and H. J. Goldsmith. Nottingham: Drs. W. S. Whimster, J. M. Macfie, and W. R. O. Gosling. Grimsby: Drs. M. Steel and D. I. Gantzer. Mansfield: Drs. J. C. Pease and J. N. Wattie. Scunthorpe: Drs. J. H. D. Millar and V. Kritzinger.

The group gratefully acknowledge the assistance of the many physicians who permitted study of their patients and of the pathologists in each hospital who provided special post-mortem reports.

The cost of printing the record cards and expenses incurred during analysis of the records were borne by the Sheffield Regional Hospital Board.

Classification of Chief Diagnostic Groups of Cases of Heart Failure

Table I shows the entire series of 487 cases, divided into the four diagnostic groups of cor pulmonale, degenerative, rheumatic, and miscellaneous cases listed by area. There were 235 patients from the Sheffield City General Hospital, of whom 96 (41%) were classified as cases of cor pulmonale, and 252 patients from elsewhere of whom 76 (30%) were cases of cor pulmonale. The total number of cases of cor pulmonale was thus 172 of 487 cases (35%). This should be compared with the totals of 165 degenerative cases

COR PULMONALE INVESTIGATION : CASE REPORT

HOSPITAL .....

PHYSICIAN IN CHARGE ..... PATIENT'S OWN DOCTOR.....

PATIENT'S NAME ..... DOCTOR'S ADDRESS .....

SEX.....AGE..... .....

HOSPITAL RECORD No. ....

RESIDENCE : Number of years in town..... Give type of area.....

Number of years in country ..... Give type of area.....

(If residence varied give main type of area, e.g. industrial, country town, colliery village, etc.)

OCCUPATIONS :	INDUSTRY OR UNDERTAKING :
Most recent	..... No. of years.....
Previous	..... No. of years.....
.....	..... No. of years.....
.....	..... No. of years.....
.....	..... No. of years.....

If the answer is " No " or " None " please cross out the appropriate word.
If the answer is " Yes " please tick. Insert figures where appropriate.

SMOKING HABITS (now if smoking : before cessation if given up)
- Most recent amount smoked :
  - No. of cigarettes per day (average) . . ..
  - Pipe tobacco, ounces per week . . ..
  - Never smoked or odd ones only . . ..
- Total number of years' smoking . . ..
- If stopped, no. of years since smoking . . ..
- Type of smoking :
  - Cigarettes only (pipe < 1 year regly.) . .....
  - Pipe only (cigarettes < 1 year regly.) . .....
  - Mixed cigarettes and pipe smoking . . . .

PAST HISTORY : Give year of onset or attack(s).
- Chest disease :
  - Asthma . . . .
  - Bronchiectasis . . ..
  - Occasional Bronchitis . .....
  - Annual " . . ..
  - Habitual " . . ..
  - Pneumonia . . . .
  - Pulmonary Tuberculosis .....
  - Silicosis . . . .
  - Scoliosis . . . .
  - Bronchial Carcinoma . .....
  - Chest operations . .....
- Rheumatic heart disease :
  - Chorea . . . .
  - Arthritis . . . .
  - Valvular . . . .
- Angina pectoris :
  - Of effort . . . .
  - At rest . . . .
- Other conditions (specify) :
  - Syphilitic .....
  - Thyroid .....
  - Renal .....
  - Congenital .....
  - Other .....
  - .....
- Previous attacks of congestive failure . . ..
  - (number) . . ..

PAST SYMPTOMS : Give year of onset if known.
- Dyspnoea (on effort) . .....
  - " (nocturnal) . .....
- Pain in chest . . . .
- Sputum . . . .
- Haemoptysis . . . .
- Oedema of ankles :
  - Intermittent . . ..
  - Persistent . . ..
- Cough :
  - Intermittent . . ..
  - Every winter . . ..
  - Habitual . . . .
- Wheezing :
  - With bronchitis . . ..
  - Habitual . . . .

PRESENT ILLNESS :
- Date of onset .....
- Date of admission to hospital.....
- Date of discharge/death.....

SYMPTOMS ON ADMISSION
- DYSPNOEA :
  - Absent . . . .
  - Present on exertion (hills) .....
  - Present on climbing stairs .....
  - Present at rest . . ..
  - Present :
    - Nocturnal attacks . .....
- COUGH :
  - Absent . . . .
  - Present . . . .
- PAIN IN CHEST :
  - Absent . . . .
  - Present, pleural . . ..
  - Present, anginal . . ..
  - Other . . . .
- SPUTUM :
  - Absent . . . .
  - Present, mucoid . .....
  - Present, white, frothy . .....
  - Present, mucopurulent .....
  - Present, purulent . .....
  - Present, bloodstained . .....
- OTHER SYMPTOMS : (Specify) .....
  - .....

SIGNS ON ADMISSION
- MENTAL STATE .
  - Alert . . . .
  - Drowsy . . . .
  - Disorientated . . ..
- CYANOSIS :
  - Absent . . . .
  - Finger nails . . ..
  - Ears . . . .
  - Lips . . . .
  - Tongue . . . .
- FINGER CLUBBING :
  - Absent . . . .
  - Moderate . . . .
  - Gross . . . .
- HANDS : *(assess when patient is warm)*
  - Cold . . . .
  - Warm . . . .
  - Hot . . . .
- FOREARM VEINS : *(assess when patient is warm)*
  - Normal . . . .
  - Constricted . . ..
  - Full . . . .
- JUGULAR VENOUS FILLING : *(inspir'n and expir'n)*
  - Not visible . . ..
  - Halfway up neck . . ..
  - To angle of jaw . . ..
  - *(assess with patient at 45° or give angle)* . . . .
- EYES :
  - Normal . . . .
  - Proptosis . . . .
  - Exophthalmos . . ..
  - Conjunct'l. chemosis . ...

SIGNS ON ADMISSION *(contd.)*
- FUNDI :
  - Normal . . . .
  - Haemorrhages . . ..
  - Exudate . . . .
  - Papilloedema . . ..
- THYROID :
  - Normal . . . .
  - Enlarged . . . .
  - Nodular . . . .
- FINGER TWITCHING :
  - Absent . . . .
  - Present . . . .
  - Tremor . . . .
- PULSE :
  - Rate per minute . . ..
  - Rhythm :
    - Regular . . ..
    - Extrasystoles . . ..
    - Fibrillation . . ..
    - " apex rate/min. .....
  - Volume :
    - Normal . . . .
    - Poor . . . .
    - Full . . . .
    - Collapsing . . ..
    - Paradoxus . . ..
    - Alternans . . ..
  - Blood Pressure :
    - Systolic . . . .
    - Diastolic . . . .
- HEART :
  - Apex beat :
    - Impalpable . . ..
    - Present, space IV . .....
    - Present, space V . .....
    - Present, space VI . .....
    - Under 3" from midline .....
    - 3"–4" from midline . .....
    - Over 4" from midline .....
  - Apical impulse :
    - Absent . . . .
    - Diffuse . . . .
    - L.V. thrust . . ..
    - R.V. thrust . . ..
  - Murmurs :
    - Absent . . . .
    - Mitral diastolic . .....
    - Aortic diastolic . .....
    - Aortic stenosis . .....
    - Pulmonary stenosis . .....
    - Basal to-and-fro . .....
    - Pericardial rub . .....
  - Other murmurs (specify).....
    - .....
  - Gallop rhythm :
    - Absent . . . .
    - Apical . . . .
    - Sternal . . . .
- LUNGS :
  - Normal . . . .
  - Emphysema . . ..
  - General bronchospasm .....
  - Basal rales . . ..
  - General rales . . ..
  - Consolidation . . ..
  - Clinical effusion R. side .....
    - " " L. side .....
    - " " both sides .....
- LIVER :
  - Not palpable . . ..
  - Palpable, no. of fingers .....
  - Pulsating . . . .
- OEDEMA :
  - Absent . . . .
  - Ankles and/or sacrum . .....
  - Legs . . . .
  - Thighs . . . .
  - Flanks . . . .
  - Ascites . . . .
- URINE :
  - Specific gravity normal .....
    - " " low . .....
    - " " high . .....
  - Albumin :
    - Absent . . . .
    - Moderate . . . .
    - Heavy . . . .
  - Casts :
    - Absent . . . .
    - Present . . . .
  - Cells :
    - R.B.C.s . . . .
    - W.B.C.s . . . .

SIGNS ON ADMISSION *(contd.)*
- BLOOD UREA :
  - Amount in mg. per 100 ml.....
- HAEMOGLOBIN :
  - Percentage . . ..
- HAEMATOCRIT :
  - Percentage . . . .
- WASSERMANN REACTION :
  - Negative . . . .
  - Positive . . . .
- ALKALI RESERVE :
  - Volumes per cent . .....
- ANY OTHER RELEVANT SIGNS :.....
  - .....
  - .....

PLEASE SUMMARISE REPORTS ON :
- ELECTROCARDIOGRAM :
  - .....
  - .....
  - .....
  - .....
  - .....
- X-RAYS :
  - .....
  - .....
  - .....
  - .....
  - .....
  - .....
  - .....
  - .....
  - .....
  - .....
  - .....

SIGNS AFTER RECOVERY :
- BLOOD PRESSURE :
  - Systolic . . . .
  - Diastolic . . . .
- OEDEMA :
  - Absent . . . .
  - If present, specify :.....
- JUGULAR VENOUS FILLING :
  - Absent . . . .
  - If present, specify :.....
- LIVER :
  - Impalpable . . ..
  - If palpable, give no. of fingers . . . .
  - Pulsating . . . .

TREATMENT :
- Restricted fluids . . ..
- Restricted salt . . . .
- Antibiotics (specify) .....
  - .....
  - .....
- Drugs (specify).....
  - .....
  - .....
  - .....
- Other (specify).....
  - .....
  - .....

CLINICAL DIAGNOSIS :
- .....
- .....
- .....
- .....
- .....

P.M. DIAGNOSIS :
- .....
- .....
- .....
- .....
- .....

FIG. 1

TABLE I.—*Diagnostic Classification of Heart Failure*

Hospital Area	Total No. Cases	Diagnostic Groups of Cases of Heart Failure							
		Cor Pulmonale		Degenerative		Rheumatic		Miscellaneous	
		No.	%	No.	%	No.	%	No.	%
Sheffield City General ..	235	96	41	76	32	46	20	17	7
Derby	85	23	27	26	31	24	28	12	14
Leicester ..	75	20	27	26	35	21	28	8	11
Nottingham ..	54	26	48	16	30	7	13	5	10
Others (Grimsby, Mansfield, Scunthorpe)	38	7	18	21	55	8	21	2	5
Total other than Sheffield ..	252	76	30	89	35	60	24	27	11
Grand total ..	487	172	35	165	34	106	22	44	9

(34%) and of 106 rheumatic cases (22%). It appears that the proportion of patients with cor pulmonale was higher in Sheffield and Nottingham than elsewhere, and was lowest in the smaller regional towns, such as Grimsby, Mansfield, and Scunthorpe.

Table II shows the distribution of the patients by age and sex irrespective of the area from which they were drawn. An excess of male patients in both the cor

TABLE II.—*Age and Sex Distribution*

Ages	Sex	Cor Pulmonale		Degenerative		Rheumatic		Miscellaneous		Total No.
		No.	%	No.	%	No.	%	No.	%	
15–24	M	—	—	1	1	—	—	—	—	1
	F	—	—	—	—	1	1	—	—	1
25–34	M	2	1	3	3	7	19	1		13
	F	—	—	2	3	5	7	2	6	9
35–44	M	11	8	2	2	14	38	1		28
	F	7	18	1	2	15	22	3	9	26
45–54	M	42	32	19	19	3	8	2		66
	F	43	34	16	25	24	35	8	25	61
55–64	M	59	44	42	41	8	22	7		116
	F	13	34	28	45	21	31	14	44	76
65–69	M	20	15	35	34	5	14	1		61
	F	5	13	16	25	3	4	5	16	29
Total	M	134	100	102	100	37	100	12		285
	F	38	100	63	100	69	100	32	100	202
Ratio ..	M/F	3·5: 1		1·6: 1		1: 1·8		1: 2·6		1·4: 1

pulmonale and degenerative groups contrasts with the excess of female patients in the rheumatic and miscellaneous groups. The ratio of 3.5 males to 1 female in cor pulmonale is lower than that of 5.4 to 1 found in the series of Sheffield patients with cor pulmonale reported by Stuart-Harris and Hanley (1957). The largest number of cases fell between the ages of 45 and 64, and the proportions by age did not differ greatly in the various diagnostic groups. It must not be forgotten that the study did not include patients aged 70 or over.

Table III records the total number and proportion of deaths and of necropsies. The overall death rate was high (35%), but was similar in the various groups. Among the 165 patients with degenerative heart disease there were 49 fatalities, 26 of which occurred in the 83 patients with hypertension only, and 19 more in patients with or without evidence of hypertension who had suffered recent myocardial infarction. Thus the death rate in patients with recent infarction was 46%, which was the highest in the series. The proportion of fatal cases on which necropsies were performed was much the same in the various groups, and was 73% of the total.

Table IV shows the underlying chest diseases and associated conditions found in the 172 cases of cor pulmonale, 96 of whom were from Sheffield and 76

TABLE IV.—*Associated Conditions in 172 Cases of Chronic Cor Pulmonale*

	96 Cases from Sheffield	76 Cases from Other Areas	172 Cases in Total
Chest Disease			
Total bronchitis and/or emphysema	92	74	166
Bronchitis and/or emphysema alone	64	38	102
Bronchiectasis	14 (3)	16 (2)	30 (5)
Kyphoscoliosis	9 (1)	3	12 (1)
Asthma	4	5	9
Pneumoconiosis and other fibrosis	4	3	7
Pulmonary embolism and thrombosis ..	2	4	6
Pulmonary tuberculosis ..	3	3	6
Carcinoma lung	2*	1	3
Bronchopneumonia ..	3	10	13
Lung abscess	—	2	2
1 case each of pneumothorax, congenital cystic lung, and Marfan's syndrome			
Other Disease			
Hypertension	16	10	26
Anaemia with Hb 70% ..	4	2	6
Ischaemic heart disease ..	4	—	4
Recent myocardial infarct	—	1	1
Rheumatic heart disease	—	2	2
1 case each of nephrosis, cystic kidney, renal calculus, chronic alcoholism, and acute glaucoma.			

* One case possibly gastric in origin.
Figures in parentheses where the condition was the sole diagnosis.

from other areas. Bronchitis and/or emphysema was present in 92 of the Sheffield patients (96%) and in 74 of the others (98%), and was the only chest disease mentioned in 64 Sheffield and 38 other patients. Bronchiectasis was present in 30 patients, and was the sole diagnosis in three Sheffield cases and two other cases. Kyphoscoliosis was noted in 12 patients, and was the sole diagnosis in one Sheffield case. Other forms of chest disease such as asthma, pneumoconiosis, pulmonary tuberculosis, pulmonary embolism or thrombosis, carcinoma, pneumonia, lung abscess, pulmonary oedema, and pneumothorax were found in small numbers of patients who also had chronic bronchitis and/or emphysema. The proportion of

TABLE III.—*Deaths and Post-mortem Examinations*

Hospital Area	Ages	Cor Pulmonale			Degenerative			Rheumatic			Miscellaneous			All		
		No.	Deaths	P.M.	No.	Deaths	P.M.	No.	Deaths	P.M.	No.	Deaths	P.M.	No.	Deaths	P.M.
Sheffield ..	<45	10	2	2	5	2	2	13	5	5	2	—	—	30	9	9
	45+	86	30	23	71	16	14	33	11	9	15	5	4	205	62	50
Other areas ..	<45	10	4	2	4	1	1	29	10	8	5	4	4	48	19	15
	45+	66	31	25	85	30	18	31	10	3	22	9	5	204	80	51
Total ..	<45	20	6	4	9	3	3	42	15	13	7	4	4	78	28	24
	45+	152	61	48	156	46	32	64	21	12	37	14	9	409	142	101
All ages ..		172	67	52	165	49	35	106	36	25	44	18	13	487	170	125
		38%			30%			34%			41%			35%		

patients with various chest diseases is similar to that found in the series of cases of cor pulmonale reported by Stuart-Harris and Hanley (1957). Associated conditions other than hypertension (26 cases) were uncommon (Table IV).

Chief Clinical Findings in Three Groups of Cases of Heart Failure

The clinical details obtained by history and by physical examination at the time of admission were of course used in classifying the patients in one or other of the diagnostic groups. The findings which were of chief differential value in the three principal groups are totalled and set out in Table V, of which section A shows the past history and symptoms on admission. Recurrent attacks of bronchitis were more than three times as common in the cases of cor pulmonale than in either of the other groups. A similar excess existed in those with a past history of asthma or of pneumonia in the cor pulmonale cases. Previous attacks of congestive failure had occurred in all the various groups of patients. Rheumatic manifestations, including chorea, arthritis, and valvular disease, occurred almost exclusively in the rheumatic cases. A past history of anginal chest pain was obtained in 45 (27%) degenerative, in 11 (6%) cor pulmonale, and in 8 (8%) rheumatic cases.

TABLE V.—*Chief Clinical Findings in Three Main Groups of Cases of Heart Failure*

	Cor Pulmonale 172 Cases		Degenerative 165 Cases		Rheumatic 106 Cases	
	No.	%	No.	%	No.	%
A. Past History and Symptoms on Admission						
Past history:						
Recurrent bronchitis	146	85	39	24	22	21
Asthma	35	20	11	7	1	1
Bronchiectasis	17	10	1	1	—	—
Pneumonia	76	44	25	15	27	26
Tuberculosis	6	3	4	2	1	1
Silicosis or pneumoconiosis	4	2	—		—	
Scoliosis or kyphoscoliosis	12	7	2	1	—	
Previous congestive failure	35	20	26	16	41	39
Rheumatic manifestations	6	3	12	7	68	64
Anginal pain	11	6	45	27	8	8
Symptoms on admission:						
Cough	154	90	107	65	74	70
Sputum: mucoid	24	14	31	19	32	30
" mucopurulent or purulent	98	57	20	12	8	8
Anginal pain	9	5	31	19	9	9
Pleural and other chest pain	23	13	25	15	20	19
B. Signs on Admission						
General:						
Drowsiness and disorientation	71	41	34	21	7	7
Cyanosis of lips	159	93	69	42	52	49
" " tongue	142	83	33	20	18	17
Clubbing of fingers	69	40	12	7	14	13
Hands cold	11	6	45	27	30	28
" hot	35	20	8	5	3	3
Conjunctival chemosis	39	23	5	3	1	1
Twitching of fingers	28	16	2	1	1	1
Peripheral circulation:						
Raised jugular venous pressure	169	98	156	95	100	95
Auricular fibrillation (pulse)	9	5	37	22	74	70
Diastolic B.P. 100 mm. Hg or more	26	15	83	50	9	9
Cardiac signs:						
Impalpable cardiac impulse	74	43	51	31	5	5
Diffuse " "	64	37	47	29	22	21
Right ventricular "	59	34	5	3	35	33
Left " "	12	7	77	47	57	54
Murmurs	17	10	68	41	105	99
Gallop rhythm at apex	25	15	49	30	11	10
" " " sternum	35	20	17	10	2	2
Electrocardiograms:						
No. done	159	100	154	100	95	100
" normal	20	13	14	9	3	3
Auricular fibrillation	8	5	26	17	70	74
P pulmonale	91	57	—	—	3	3
Right ventricular strain	64	40	—	—	14	15
Left " "	11	7	69	45	27	29
Chest signs:						
Clinical emphysema	147	86	36	22	7	7
"Bronchospasm"	108	63	31	19	12	11
X-rays done	149	100	144	100	93	100
X-ray suggestive of emphysema	72	48	14	10	2	2
" " other chronic lung disease	34	23	10	7	2	2

The symptoms present on admission and listed in Table V are selected because of their differential value, and dyspnoea, which was present in almost all of the patients, is omitted. Cough was present in two-thirds or more of the patients in each group. A mucoid sputum was of no differential value, but a mucopurulent or purulent sputum was more than four times as common in the cases of cor pulmonale. Chest pain other than angina was, however, of little differential value; anginal pain was naturally commoner in the degenerative cases, and was present on admission in 31 cases (19%).

Section B of Table V gives the principal physical signs at the time of admission. The high incidence in cor pulmonale cases of cyanosis of the lips (93%) and of the tongue (83%) is particularly noteworthy. Cyanosis of the lips was present in only half of the patients with degenerative or rheumatic disease, and the tongue was noted to be cyanotic in only one-fifth of these patients. Warm peripheral extremities, chemosis of the conjunctivae, and twitching of the fingers, which are often regarded as of diagnostic value in cor pulmonale, were present in less than one-quarter of these patients, yet were even less common in the other groups. A drowsy or mentally disorientated state was, however, present in 40% of the patients with cor pulmonale and was twice as common in these as in the other groups of patients.

Some findings in regard to the heart and peripheral circulation deserve special comment. 95% or more of the patients had a raised jugular venous pressure on admission, and therefore there were few patients admitted to the series on the basis of hepatomegaly without raised venous pressure in the neck. In the cases of cor pulmonale the cardiac rhythm was usually regular, but auricular fibrillation was present in nine patients. Auricular fibrillation occurred more frequently in the patients with hypertension or ischaemic disease, yet it was found in only 22% compared with 70% of the rheumatic cases. A diastolic blood pressure in excess of 100 mm. Hg was present in half of the cases of degenerative disease, compared with 15% of cor pulmonale and 9% of rheumatic cases. When palpable the cardiac impulse was usually right ventricular in type in cor pulmonale, left ventricular in degenerative cases, and right or left (or both) in rheumatic disease. Murmurs were of course a feature of valvular disease and were uncommon in cor pulmonale, but a gallop rhythm was equally common in degenerative and cor pulmonale cases.

It proved difficult to analyse the electrocardiograms in a statistical form, and, in any case, these were not taken in patients who succumbed soon after admission. No attempt was made to code the findings of right or left ventricular hypertrophy. Of the 408 patients on whom reports were available, 37 were stated to have normal electrocardiograms, and these included some patients from each group. A "P pulmonale" wave and right ventricular strain pattern were the chief abnormalities in cor pulmonale. A left ventricular strain pattern was characteristic of hypertension, and the changes usually interpreted as being due to

ischaemia were almost confined to the degenerative group.

Physical signs in the chest which suggested emphysema were found in 86% of the patients with cor pulmonale and were also present in 22% of the degenerative cases. Radiographic appearances suggestive of emphysema were present in 48% of those cases of cor pulmonale in whom *x*-ray films of the chest were available and in 10% of the degenerative cases. Radiological evidence of other chronic lung disease was found in 23% of the cor pulmonale cases and in 7% of the degenerative cases. Clinical evidence of "bronchospasm" was predominantly found among the cases of cor pulmonale, and it was recorded in 63% of these, compared with 19% of degenerative cases and 11% of rheumatic cases.

The Blood

The results of the estimation of the haemoglobin, the haematocrit, the blood urea, and the plasma alkali reserve are shown in Table VI and in Fig. 2. In spite of the many different laboratories concerned and the fact that only some of the patients were tested, the results show both similarities and differences between the various groups of cases. The latter are considered in only three groups—cor pulmonale, degenerative, and rheumatic and miscellaneous—and the distribution of the results is shown in percentages.

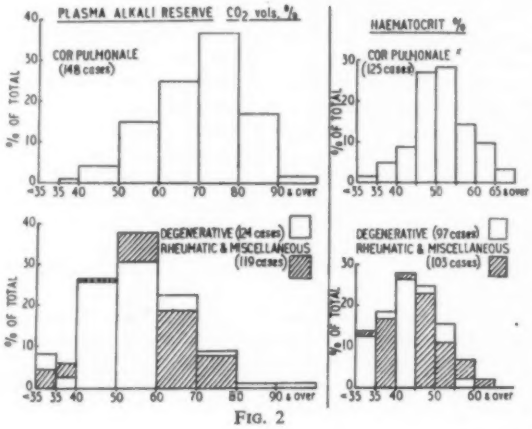

FIG. 2

The variation in the haemoglobin was considerable in each group of cases. The highest number of patients with a haemoglobin of less than 70 occurred in the miscellaneous group, in which were placed cases of anaemia without other evidence of heart disease. Nevertheless each group included some anaemic cases, and these patients had sometimes suffered from gastro-intestinal haemorrhage or long-standing nephritis. The distribution of the haematocrit percentages was remarkably similar in the degenerative and combined rheumatic and miscellaneous cases, about half of whom had values which lay between 40 and 50%. The haematocrits of the cor pulmonale cases were often higher, and 57% of results fell between 45 and 55%. 27% of the cor pulmonale cases had haematocrits in excess of 55%, compared with only 9% of the rheumatic and miscellaneous cases and 2% of the degenerative cases. The haematocrit distribution in cor pulmonale was similar to that recorded by Stuart-Harris and Hanley (1957).

The blood urea was often elevated in all forms of heart failure, and normal values of less than 40 mg. per 100 ml. were present in only 41% of cor pulmonale, 32% of degenerative cases, and 39% of rheumatic and miscellaneous cases. There were a few more cases in the degenerative than in the other groups with a blood urea in excess of 90 mg. per 100 ml., probably because of the inclusion of cases with nephritis in this category.

The venous plasma alkali reserve is a poor substitute for the arterial carbon dioxide content or tension. Nevertheless, as Table VI and Fig. 2 show, the distribution of the alkali reserve was much the same in

TABLE VI

Haemoglobin (%)

Group	Total No.	<60		60–69		70–79		80–89		90–99		100–109		110–119		120+	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Cor pulmonale	157	3	2	3	2	15	10	30	20	49	31	35	22	17	10	5	3
Degenerative	150	11	7	10	7	25	17	35	23	39	26	18	12	9	6	3	2
Rheumatic and miscellaneous	140	15	11	13	9	17	12	35	25	26	19	22	16	9	6	3	2

Haematocrit (%)

		<35		<35–39		40–44		45–49		50–54		55–59		60–64		65+	
Cor pulmonale	125	2	2	6	5	11	9	34	27	38	30	18	14	12	10	4	3
Degenerative	97	12	12	18	18	26	27	24	25	15	15	2	2	0	0	0	0
Rheumatic and miscellaneous	103	14	14	17	17	28	27	24	22	11	11	7	7	2	2	0	0

Blood Urea (mg. per 100 ml.)

		<30		<30–39		40–49		50–59		60–69		70–79		80–89		90+	
Cor pulmonale	146	28	19	32	22	40	27	17	12	11	8	3	2	1	1	14	10
Degenerative	147	19	13	28	19	33	23	16	11	13	9	9	6	4	3	25	17
Rheumatic and miscellaneous	126	27	21	23	18	33	26	21	17	5	4	2	2	1	1	14	11

Plasma Alkali Reserve (Volumes %)

		<35		<35–39		40–49		50–59		60–69		70–79		80–89		90+	
Cor pulmonale	148	0	0	1	1	6	4	22	15	37	25	55	37	25	17	2	1
Degenerative	124	10	8	3	2	32	26	38	30	28	22	11	9	1	1	1	1
Rheumatic and miscellaneous	119	5	4	7	6	31	26	45	38	22	19	9	8	0	0	0	0

degenerative and combined rheumatic and miscellaneous groups, and differed from that in the cases of cor pulmonale.

In the degenerative and combined rheumatic and miscellaneous groups 78 and 83% respectively of the values for the alkali reserve lay between 40 and 70 volumes %. There were 11 and 8% of values in excess of 70 volumes % in these cases. But in the cor pulmonale cases only 44% of values lay between 40 and 70 volumes % and 55% were in excess of 70 volumes %. The fact that there were so many high values in the cor pulmonale cases is doubtless explained by the state of respiratory acidosis and carbon dioxide retention in this condition, known from the work of many authors (Baldwin *et al.*, 1949; Platts, 1953).

Therefore both a high haematocrit and a raised plasma alkali reserve may be of differential value in the diagnosis of cor pulmonale, particularly when it is not possible to obtain an analysis of the arterial blood oxygen saturation or carbon dioxide tension.

Relative Frequency of Certain Personal Characters

The record form used during this inquiry contained sections on the duration of residence in various areas, on the present and previous occupations, and on smoking habits. Such information required co-operation from the patients, which could not be given by severely ill or dying patients. It has already been shown (Stuart-Harris and Hanley, 1957) in a symptomatic inquiry carried out in Sheffield by Dr. Marjorie Clifton that the symptoms of bronchitis are correlated less well with the present work of a group of men in industry than with previous work which entailed exposure to dust. For this reason much more careful inquiry of past occupations would have been necessary for valid correlations between the type of occupation and variety of heart failure than that of the present study. It was in fact found that a very large number of occupations had been pursued by the 285 men in the present inquiry. The record of past occupations was not always complete, the degree of exertion and exposure to dust in the various jobs were matters of surmise, and detailed analysis and correlations were therefore abandoned.

The question of residence in various areas was considered by first separating those who had lived primarily in an industrial environment. There were relatively few who had lived in other areas, including rural dwellers and those living in county towns or a seaport such as Grimsby. Data on 339 patients from an industrial environment and 119 from rural and other urban areas were available and are shown by diagnostic classification in Table VII. The patients from Sheffield and Nottingham hospitals were largely resident in an industrial area, the ratio of industrial to other dwellers being 8.6:1 and 6.1:1 respectively. Elsewhere the numbers of industrial and of other dwellers bore a closer relation to each other (1.5:1). The relative proportions of patients from industrial and other areas show slight differences according to the clinical group. More of the industrial dwellers suffered from cor pulmonale (39%) than from any other form of heart failure in both Sheffield and other hospitals, whereas in those living in other types of area and mostly resident elsewhere than Sheffield, degenerative heart failure preponderated (36%). However, the differences are too small to establish a correlation between environment and disease. In any future inquiry many more patients living in a purely rural area should be examined in order to establish evidence concerning this matter.

Finally, the smoking habits recorded in 256 men and 191 women are considered in Table VIII. The number of heavy and moderate smokers among the women was only 35, and was too small for a comparison between smoking habits and the incidence of the various forms of heart failure. There were 30 men who had never smoked and 40 who smoked a pipe only or who had given up cigarette smoking. Moderate cigarette smokers (1–15 a day) totalled 113, and 82 men were heavy smokers (more than 15 cigarettes daily). The distribution of patients according to smoking habits shows an excess of heavy cigarette smokers in cases of cor pulmonale. Thus there were 44 heavy smokers among 134 such patients (33%), compared with only 7 heavy smokers among 49 (14%) rheumatic and miscellaneous cases.

A similar proportion of heavy smokers was noted among the cases of degenerative heart disease, and this

TABLE VII

Type of Residential History	Sheffield			Regional Total			Total		
	Indust.	Other	No Record	Indust.	Other	No Record	Indust.	Other	No Record
Cor pulmonale	80	9	7	52	20	4	132 (39%)	29 (24%)	11
Degenerative	68	5	3	46	38	5	114 (34%)	43 (36%)	8
Rheumatic	38	7	1	30	24	6	68 (20%)	31 (26%)	7
Miscellaneous	12	2	3	13	14	—	25 (7%)	16 (14%)	3
Total	198	23	14	141	96	15	339 (100%)	119 (100%)	29
Ratio (indust./other)	8·6:1			1·5:1			2·8:1		

TABLE VIII.—*Smoking Habits in 285 Male Cases of Heart Failure*

	Never Smoked		Pipe Only or Given Up Cigs. > 5 Years		Cigarettes 1–15/Day		Cigarettes Over 15/Day		No Record of Smoking Habits		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Cor pulmonale	12	9	19	14	52	39	44	33	7	5	134	100
Degenerative	11	11	16	16	38	37	31	30	6	6	102	100
Rheumatic and miscellaneous	7	14	5	10	23	47	7	14	7	14	49	100
Total*	30	11	40	14	113	40	82	29	20	7	285	100
All groups of female cases	152	75	4	2	31	15	4	2	11	5	202	100

* When tested by the χ^2 test (with 4 degrees of freedom) the significance of the association between smoking and the clinical classification is such that it could occur once in five times ($p = 0{\cdot}20$) by chance.

was further studied by subdivision according to the presence or absence of ischaemia in the cases of hypertension. Of 40 hypertensive patients 11 were heavy smokers, compared with 20 of 62 patients with ischaemia. Too much reliance cannot be placed on this slight difference, but the total number of 31 heavy smokers (30%) represents an excess compared with the figure for rheumatic and miscellaneous cases. In neither cor pulmonale nor ischaemic disease was the association with smoking statistically significant.

Discussion

The clinical features of chronic anoxic cor pulmonale which are usually accepted as being essential for the diagnosis are, first, the central cyanosis visible in the tongue and warm extremities; secondly, the presence of an acute chest infection superimposed on chronic lung disease; and, thirdly, right ventricular disease with hypertrophy or electrocardiographic strain in the absence of other causes such as pulmonary embolism, or congenital or valvular heart disease. To these many would add evidence from arterial blood examination of unsaturation with oxygen and a high carbon dioxide tension. These features have not usually been sought by simultaneous study of other forms of congestive failure, and the present investigation has achieved this in a statistical way.

The figures already given for the relative frequency of cyanosis of the lips and tongue, of drowsiness or disorientation, of mucopurulent or purulent sputum, of a past history of bronchitis, of physical signs suggestive of emphysema with obstructed breathing and the various cardiac signs show that there is a distinctive clinical picture which can be recognized by many observers working in different hospitals. Moreover, auricular fibrillation, left ventricular disease, and hypertension are usually absent in cor pulmonale except for a small percentage of patients in whom combined disease may exist. When to the clinical features is added the help given by the venous haematocrit and plasma alkali reserve it appears that confirmation of the diagnosis is open to all with reasonable facilities for clinical investigation.

This study has shown the unquestionable numerical importance of cor pulmonale in the main hospital centres of one region. Yet the limitation of a purely hospital study in areas of a generally similar character is obvious. The rural county of Lincolnshire, for instance, supplied few patients to this study largely because patients with heart failure in country districts tend to be treated at home. The overall prevalence of cor pulmonale in hospital was 35%—a figure even higher than that recorded by Flint (1954). The disease was largely found in males and in those suffering from chronic bronchitis and emphysema. Its frequency may be due to the large size of the problem of this form of chest disease in the areas concerned. If this study had been designed as an epidemiological investigation regions of a more diverse character and with other forms of chest disease, such as tuberculosis or pneumoconiosis, would have been interesting to study. The data concerning the patients' residence are indicative of a general relation between cor pulmonale and life in an industrial environment, as has previously been shown for chronic bronchitis (Stuart-Harris and Hanley, 1957). That rural populations might provide contrasts is obvious. Yet in Belgrade, Slavković *et al.* (1955) found that cor pulmonale was present in 16.7% of 265 cases of heart failure and a majority of the patients with cor pulmonale were performing heavy manual work out of doors, many being farmers.

The effect of heavy cigarette smoking on the prevalence of respiratory symptoms is well known, and is again apparent in the cases of cor pulmonale, though the association is not statistically significant. The present findings agree with the association of heavy smoking with bronchitis found by several authors (Doll and Hill, 1956; Stuart-Harris and Hanley, 1957; Edwards *et al.*, 1959; Higgins, 1959). A similar association between heavy smoking and ischaemic heart disease has been suggested by Hammond and Horn (1954), and among doctors of certain ages by Doll and Hill (1956). Hammond and Horn (1958) and Buechley *et al.* (1958) have confirmed this relationship. Yet no gradation in the prevalence of ischaemic disease in various classes of smokers was found in the Framingham heart study by Dawber *et al.* (1957), and Edwards *et al.* (1959) have recorded a negative relationship between hypertension and smoking. Our own results were on the whole suggestive of a positive relationship between ischaemic disease and smoking habits.

Summary

487 cases of congestive heart failure admitted to hospitals of the Sheffield hospital region were studied during 1955 and 1956. 235 patients were from Sheffield, most of the remainder being admitted to hospitals in Derby, Leicester, and Nottingham. The cases were classified into four groups—cor pulmonale, degenerative, rheumatic, and miscellaneous.

The proportion with cor pulmonale in Sheffield was 41% and in the other hospitals 30%. Hypertension and ischaemic heart disease occurred in 32% of Sheffield cases and in 35% of cases in other areas. Rheumatic heart disease and a number of miscellaneous conditions, such as anaemia, thyroid disease, pulmonary embolism, congenital heart disease, acute infections, carcinoma, and obesity, made up the remainder.

The age and sex distribution of the cases of cor pulmonale indicated a preponderance in males aged 45 to 64, but patients of 70 and over were not included in the study.

The death rate was from 30 to 41% in the various groups of cases, with an overall rate of 35%. The rate for patients with recent myocardial infarction was 46%.

Patients with cor pulmonale had a high incidence of past attacks of bronchitis and of pneumonia and a low incidence of rheumatic manifestations and of anginal pain.

At the time of admission the expectoration of mucopurulent or purulent sputum, drowsiness or disorientation, cyanosis of the lips or tongue, clubbing of the fingers, chest signs suggesting emphysema, and evidence of right ventricular disease occurred to a much greater extent in cases of cor pulmonale than in the other groups of cases. Auricular fibrillation, left ventricular disease, and hypertension occurred in a lower percentage in cor pulmonale than in other cases.

A raised venous haematocrit and high plasma alkali reserve occurred more often in cases of cor pulmonale than in the other groups.

Residence in an industrial environment was commoner in the cor pulmonale cases than was residence in other areas.

Heavy cigarette smoking was associated with both cor pulmonale and degenerative heart disease, but the association might have occurred by chance.

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MANNOMUSTINE IN TREATMENT OF LEUKAEMIAS, POLYCYTHAEMIA, AND MALIGNANT DISORDERS

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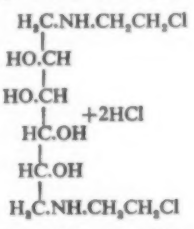
Since the introduction of β-chloralkylamines as therapeutic agents for the treatment of leukaemias and the reticuloses (Gilman and Philips, 1946; Wilkinson and Fletcher, 1947) many derivatives and analogues have been examined. Those in more or less regular use at the present time have been considered previously (Wilkinson, 1953, 1955a, 1955b; Scott, 1958). Another cytostatic preparation that has been tried more recently is mannomustine (1:6 - bis(β - chloroethylamino) - 1:6 - desoxy - D - mannitol dihydrochloride; B.C.M.; "degranol"), a substance synthesized by Vargha as one of a series of compounds linking the actively cytotoxic chemical group β-chlorethylamine with a naturally occurring substance, mannitol; it was thought that this would pass more readily through the cell membrane and therefore have a greater selectivity (Vargha *et al.*, 1957).



Mannomustine is a white crystalline compound readily soluble in water, and, although it remains stable for at least 24 hours, it should preferably be freshly prepared immediately before injection. There are a few reports of the therapeutic trial of this substance by Sellei *et al.* (1956) and by Sellei and Eckhardt (1958) at the National Oncological Institute, Budapest.

Through the kindness of Messrs. Leda Ltd., generous supplies of mannomustine have been made available to us. We report here our preliminary results with this drug in 45 patients having polycythaemia, leukaemias, reticuloses, or malignant disease.

Dosage and Control

Mannomustine was supplied in ampoules containing 50 mg. of the dry crystalline substance; for use the contents of the ampoule or ampoules were dissolved in either physiological saline or ascorbic acid solution (10 g./100 ml.); a convenient strength was 10–20 mg. of mannomustine per ml., although concentrations of 25–40 mg./ml. have been given without the development of thrombophlebitis. It was given intravenously in most cases, but we have also injected the solution intrapleurally when there has been a massive or persistent pleural effusion.

Since the administration of doses as high as 200–500 mg. in one injection led to the much greater frequency and severity of toxic reactions, we later restricted the maximal single dose to 100 mg. daily or on alternate days, and this was found to be the most satisfactory dosage scheme. The required total dosage varied from patient to patient and with the particular disease, as we indicate later.

Diagnoses were made on the usual basis of history, clinical findings, and examination of peripheral blood and bone marrow in the leukaemias and polycythaemia, and in addition by gland biopsy in the reticuloses. Haemoglobin levels and total white blood cell and platelet counts were measured daily and full blood counts at weekly intervals on in-patients and full blood counts were taken at each out-patient attendance.

Chronic Myeloid Leukaemia (12 Cases)

Twelve patients with chronic myeloid leukaemia were treated with mannomustine (see Table I). Nine of these had had no previous antileukaemic treatment, while the remaining three (Cases 10, 11, and 12) had previously received busulphan ("myleran").

In general it was found quite satisfactory to give in single intravenous doses of 100 mg. an initial total course of 800–1,000 mg. when the initial white-cell count was 80,000 to 150,000/c.mm., and of 1,200–1,800 mg. when the initial white-cell count was over 200,000/c.mm. Subsequent doses were determined according to the haematological responses obtained.

In all patients moderate symptomatic improvements were noted, and were usually most pronounced two to six weeks after the beginning of treatment. In five patients this could be attributed partially to blood transfusions given. The livers were enlarged initially in 10 patients, 8 of whom showed moderate or marked reductions in size, maximal reductions occurring within six to eight weeks. The spleens were enlarged in all but one patient (Case 12); there was marked reduction in size in five patients; slight or moderate shrinkage in four others, and the spleen became impalpable in only two (Cases 2 and 5). One patient (Case 10) with gross splenomegaly and a white blood cell count of 31,000/c.mm. was given mannomustine in an attempt to reduce the size of the spleen. Only slight reduction

occurred, but the patient did not require further antileukaemic treatment before she died, nine months later.

The haemoglobin levels increased significantly in seven patients at an average rate of 2.5 g./100 ml. in 6.7 weeks (3–12 weeks). The initial total white-cell count varied from 27,000 to 508,000 per c.mm.; the lowest values were usually recorded after four to six weeks from the beginning of treatment (see Table I). Further rises to higher levels usually occurred within a further four to five weeks, with the exception of one patient (Case 1) who is still in remission after eight months. There was no reduction in the percentage of early myeloid cells in three patients, while in the remaining nine the percentage of primitive cells varied directly with the total white-cell count. The greatest reduction was noted in the "blast" forms, the less immature early myeloid cells being more resistant. Only two patients developed thrombocytopenia, both symptomless and transient. Further courses of mannomustine were given in six cases (Nos. 2, 3, 5, 6, 9, and 12). The response to these second courses was disappointing in all six, three showing no response, while the remaining three, after a preliminary improvement, relapsed four to five weeks later.

Case 1.—A 63-year-old woman with chronic myeloid leukaemia was given mannomustine to a total of 800 mg. (100 mg. on alternate days). The white blood cells fell from 117,000 to 1,050/c.mm. in four weeks. Simultaneously the platelets fell from 256,000 to 30,000/c.mm. and the haemoglobin from 9.2 g./100 ml. (62%) to 5.9 g. (40%). She was given blood transfusions and prednisolone, 40 mg. daily, and within seven days the white blood cells and platelets had risen to normal levels. Four weeks later the white blood cells were 23,000/c.mm. and a further 50 mg. of mannomustine was given. The white blood cells remained below 20,000/c.mm. for 36 weeks without further treatment. There was a 25% reduction in the size of the liver and the spleen over the first 11 weeks, but no further change occurred.

Case 2.—A 54-year-old man with chronic myeloid leukaemia had a moderately enlarged liver and spleen; total white blood cells, 151,000/c.mm.; haemoglobin, 8.6 g./100 ml. (58%); and platelet count 250,000/c.mm. He was given mannomustine, 100 mg. daily, to a total of 1,200 mg. In six weeks the white blood cells had fallen to 4,600/c.mm., haemoglobin rose to 11.1 g. (75%), and the liver and spleen were not palpable. The platelet count remained above 150,000/c.mm. He relapsed four weeks later, the spleen and liver enlarging and the total white blood cells rising to 119,000/c.mm. A further course of 750 mg. of mannomustine was given, with partial regression of liver and spleen and a fall in the white blood cells to 34,000/c.mm. He again relapsed four weeks later, and was subsequently controlled on busulphan.

Seven of the 12 patients (Cases 2, 3, 4, 5, 7, 8, and 9) were subsequently adequately controlled on busulphan: three (Cases 6, 10, and 12) died in an acute myeloblastic phase. Case 1 has not required any further antileukaemic treatment, and one patient (Case 11) who had previously become resistant to busulphan has been treated subsequently with demecolcine.

TABLE I.—*Effect of Mannomustine in Chronic Leukaemias*

Case No.	Age and Sex	Total Dose mg. (mg./kg.)	Before Treatment: Clinical Condition	Before Treatment: W.B.C. 10^3/c.mm.	After Treatment: Clinical Condition	After Treatment: W.B.C. 10^3/c.mm.	After Treatment: Weeks	Duration of Response (Weeks)
			Chronic Myeloid Leukaemia					
1	63 F	850 (16·7)	Poor S++++ L+++	117	Fair† S+++ L++	1·05	4	36•
2	54 M	1st course 1,200 (17·3)	Fair S+++ L++	151	Good S 0 L 0	4·6	6	4
		9 wks. later 750 (10·4)	Fair S++++ L++	119	Fair S++ L+	34	5	4
3	37 F	1st course 1,200 (22·6)	Fair S++++	451	Fair S++	139	6	3
		4 wks. later 1,300 (24·4)	Good S+++	338	Good S+++	174	4	—
4	26 M	1,300 (21·1)	Fair S++++ L+	482	Good S++† L 0	44	6	2
5	59 F	1st course 1,000 (20·4)	Poor S+++	154	Fair S 0†	21	5	14
		10 wks. later 400 (8·2)	Fair S+	72	Fair S++	114	2	—
6	58 F	1st course 1,100 (20·4)	Fair S++++ L+++	257	Fair S++ L+++	52	6	5
		10 wks. later 1,400 (25·3)	Fair S++++ L+++	109	Fair S++++ L+++	32	6	4
7	39 M	1,400 (26·7)	Fair S+++ L+	259	Good S++ L 0	40·4	3	3
8	53 F	800 (16·0)	Good S++++ L+	80	Good S++ L 0	12	7	7
9	45 M	1st course 1,800 (30·0)	Poor S++++ L++	508	Fair† S+ L 0	27	6	2
		8 wks. later 1,000 (16·6)	Fair S++ L+	212	Fair+ S++ L 0	181	6	—
10	49 F	1,200 (21·8)	Poor S++++ L++	31	Poor S++++ L+	4·25	4	—
11	52 F	1,000 (13·8)	Good S++++ L+++	160	Good S+++ L++	33	4	1
12	27 F	1st course 150 (2·3)	Good L+	27	Fair† L+	8·9	9	4
		5 wks. later 600 (9·5)	Fair L+	225	Fair L+	28	3	5
			Chronic Lymphatic Leukaemia					
13	57 M	1,200 (21·4)	Poor S+++ L+++ P.G.++ M.G.++	180	Fair S++ L++ P.G.+ M.G.++	150	3	—
14	62 F	700 (9·3)	Good S+ P.G.++	168	Good S 0 P.G. 0	4·3	3	40•
15	57 M	700 (9·0)	Good S+ P.G.++	262	Good S+ P.G.+	22·7	2	18•

S=Size of spleen. L=Size of liver. P.G.=Peripheral glands. M.G.=Mediastinal glands.
• Continuing. † Given blood transfusions.

Chronic Lymphatic Leukaemia (3 Cases)

Three patients with chronic lymphatic leukaemia were treated with mannomustine (see Table I). One patient (Case 13) was in poor general condition before treatment, having considerable enlargement of liver and spleen and widespread involvement of all the lymph nodes. The other two patients were in reasonably good general health with moderate enlargement of lymph nodes and barely palpable spleens. The initial total white-cell counts varied between 168,000 and 262,000/c.mm., while the platelet counts were between 195,000 and 218,000/c.mm.

The responses to treatment varied considerably; in spite of a total dose of 1,200 mg. given in Case 13, the total white-cell count remained high and the liver, spleen, and lymph nodes showed only slight reduction in size. He developed severe thrombocytopenia (less than 50,000/c.mm.) resulting in fatal haemorrhage despite blood transfusions. Cases 14 and 15 had total doses of 700 mg. of mannomustine. Within three weeks one patient (Case 14) was in complete remission, which has continued for the past nine months, while the other gave only a partial remission, with a transient thrombocytopenia. No significant change in the haemoglobin from its initial normal level was noted in either patient.

Acute Leukaemia (6 Cases)

During the period of this trial we had available in our group of acute leukaemias six patients with high initial white-cell counts—three had acute monocytic leukaemia, one had acute myeloid leukaemia, one an acute lymphoblastic termination of an aplastic anaemia, and one an acute erythroid myelosis.

To each of these patients mannomustine was given in single doses of 100 mg. on alternate days for two to five doses in order to reduce the total white-cell counts to

TABLE II.—*Effect of Mannomustine in Acute Leukaemia*

Case No.	Age and Sex	Type	Before Treatment		Total Dose (mg.) 1st Course	After 1st Course		Days after Treatment	Duration of Response to 1st Course (Months)
			W.B.C. 10^3/c.mm.	% Primitive Cells		W.B.C. 10^3/c.mm.	% Primitive Cells		
16	40 M	Monocytic	54·5	88·5	400	9·5	76·5	14	2
17	49 M	"	116·0	93·0	450	9·1	81·0	10	2 (died)
18	67 F	"	64·0	34·5	200	8·2	28·5	5	2
19	52 M	Lympho-blastic	91·0	92·0	200	29·4	53·0	9	—
20	35 M	Myeloid	160·0	73·0	500	29·4	28·5	11	1
21	22 F	Erythro-myelosis	102·0	74·0	200	31·0	64·5	11	1

TABLE III.—*Effect of Mannomustine in Hodgkin's Disease*

Case No.	Age and Sex	Total Dose mg. (mg./kg.)	Before Treatment				After Treatment				Duration of Response (Months)
			Clinical Condition	Hb g./100 ml.	W.B.C. 10^3 c.mm.	Plts. 10^3/c.mm.	Clinical Condition	Hb g./100 ml.	W.B.C. 10^3 c.mm.	Plts. 10^3/c.mm.	
22	48 M	700 (12·1)	Good P.G.++	14·5	8·8	103	Good P.G. 0	14·5	6·1	202	8*
23	14 M	1st course: 900 (20·7)	Fair P.G.+++ M.G.+++	11·1	5·8	236	Fair P.G. 0 M.G. 0	6·7	0·8	40	3
		12 wks. later: 600 (13·8)	Fair P.G.+++ M.G.+++ S+	7·4	2·2	145	Fair P.G. 0 M.G. 0 S 0	†	1·1	52	3*
24	76 F	700 (16·4)	Fair P.G.+ S++++ L++++	11·3	10·2	145	Good P.G. 0 S 0 L+	12·0	4·5	164	5*
25	32 M	900 (15·5)	Good Pruritus+++ P.G.++	14·0	7·5	256	Good Pruritus 0 P.G. 0	13·3	3·7	73	4*
26	28 F	1st course: 1,000 (15·9)	Fair Pruritus++ M.G.+++ Collapsed L.L. lobe	13·9	10·4	317	Good Pruritus 0 M.G. 0 L.L. lobe re-expanded	10·2	0·8	40	3½
		14 wks. later: 650	Fair M.G.+++ L. pleural effusion	13·3	8·9	205	Good M.G.+++ Effusion aspirated	11·2	3·5	37	2*
27	28 F	1st course: 700 (12·7)	Fair Pyrexial P.G.+++	12·7	7·5	210	Good P.G.+ Afebrile	9·7	2·8	148	1½
		7 wks. later: 300 (5·4)	Fair P.G.+++	10·2	4·7	175	Good P.G.+++	10·5	2·8	176	1
28	61 M	1,050 (14·5)	Good P.G.+++	14·2	4·2	157	Good P.G.+++	11·5	5·0	100	4
29	53 M	1st course: 900 (15·0)	Good P.G.++ S+	14·6	5·3	215	Good P.G.+ S 0	10·8	4·8	215	2½
		11 wks. later: 600 (10·0)	Good P.G.++	11·8	4·6	192	Good P.G.+	10·8	5·1	148	5
30	60 M	1,000 (14·3)	Poor P.G.++	8·9	8·4	222	Poor P.G.+	†	2·8	39	1½
31	26 M	700 (11·7)	Fair Pyrexia P.G.+ M.G.++	12·1	21·0	340	Good Afebrile P.G. 0 M.G.++	10·4	9·4	86	3*

P.G.=Peripheral glands. M.G.=Mediastinal glands. S=Size of spleen. L=Size of liver. * Continuing. † Given blood transfusions.

relatively normal levels and therefore facilitate the subsequent action of prednisolone and blood transfusions. This was achieved in all six patients (Table II). In Cases 16, 18, 20, and 21 subsequent relapses with rising total white-cell counts responded to further short courses of mannomustine. The remaining two patients died in acute relapse before further courses could be effective. Five of the patients improved with the combined therapy, in Case 16 complete regression of skin nodules, splenomegaly, and lymphadenopathy being obtained. One patient with acute lymphoblastic leukaemia died 11 days after the beginning of mannomustine injections. In none of the patients was complete remission obtained.

Reticuloses (14 cases)

Hodgkin's Disease

Ten patients with Hodgkin's disease were treated with mannomustine (see Table III). Two (Cases 28 and 29) had previously been treated with " thiotepa " and/or tri-(β-chloroethyl)amine hydrochloride (" trillekamin ") with satisfactory remissions of two years and 15 months respectively. The initial total doses of mannomustine given have varied between 700 and 1,050 mg., according to the severity of the disease. Complete regressions of lymphadenopathy and/or splenomegaly were obtained in five patients and partial regressions in the remainder, in two of whom the responses were very poor. The duration of responses to the first course varied from six weeks to eight months, and second courses were given to four patients, the lymphadenopathy again showing regression in two of them.

After being maintained for six to seven weeks the haemoglobin levels fell suddenly in six patients (Cases 23, 26, 27, 28, 29, and 31), but subsequently showed improvement within three weeks. Neutropenia was noted in five patients (Cases 23, 25, 26, 27, and 30) after five to six weeks, and in Cases 23 and 26 it was severe, the total white cells being below 1,000/c.mm. Thrombocytopenia, maximal after four to five weeks, occurred in five patients; it was symptomless and transient in four (Cases 23, 25, 26, and 31), while in one (Case 30), who was in the terminal stage of the disease, the thrombocytopenia had persisted for the seven weeks before he died. The value of mannomustine in the management of Hodgkin's disease is illustrated in the following examples of cases responding to treatment.

Case 22.—A 48-year-old man presented with enlarged cervical and axillary glands. Biopsy showed typical Hodgkin's disease. He was given mannomustine, 100 mg. daily, to a total of 700 mg. Complete regression of the glands occurred within three weeks. The blood picture remained normal. There has been no recurrence over eight months.

Case 23.—A 14-year-old boy had enlarged cervical and mediastinal glands. Biopsy showed Hodgkin's disease. He was given mannomustine, 300 mg. daily, to a total of 900 mg. All glands had completely regressed in two weeks. Within four weeks he had developed a pancytopenia with agranulocytosis and was given prednisolone, 30 mg. daily, for three weeks. The white blood cells and platelet counts returned to normal levels within two weeks, the red blood cell count and haemoglobin responding more slowly. He relapsed within three months, and a second course of mannomustine, 100 mg. on alternate days, to a total of 600 mg. was given. Complete regression of all glands again occurred within two weeks and continued to the time of writing (three months). He developed an aplastic anaemia which has failed to improve with prednisolone, but he was being maintained satisfactorily by transfusions.

Case 24.—A 76-year-old woman had gross enlargement of the liver and spleen and enlarged cervical glands. Biopsy showed Hodgkin's disease. She was given 100 mg. of mannomustine daily to a total of 700 mg. Complete regression of the spleen and marked reduction in hepatomegaly occurred in six weeks; the blood count remained normal, but four months later the spleen was again just palpable.

Brill-Symmers Disease

Two patients with follicular lymphoreticulosis were treated with mannomustine. One with gross hepatomegaly and obstructive jaundice was given single injections of 500 mg. on alternate days to a total of 1,000 mg. Rapid regression of the hepatomegaly, and relief of the obstructive jaundice occurred within 10 days, the only toxic effect being a transient thrombocytopenia. She relapsed two months later and died. The second patient was confined to bed with severe lumbar pain due to spinal-nerve-root compression. He was given a total of 800 mg. of mannomustine in 100-mg. daily doses. Complete relief of all symptoms and signs of compression occurred within four weeks, and he has been fully ambulant and working for the past four months. He showed a mild transient anaemia and thrombocytopenia.

Reticulosarcoma

Mannomustine has been given to two patients with reticulosarcoma. In a man aged 57, who received two courses of mannomustine to a total of 1,000 mg. and 1,750 mg. respectively, the only beneficial effect noted was a temporary regression of the glands and extensive secondary skin nodules following the second course of mannomustine, but the massive total chemotherapeutic treatment given, which had also included trillekamin, failed to halt progression of the disease, and resulted in the production of a profound aplastic anaemia after 21 weeks, with death eight weeks later. Complete regression of the marked cervical lymphadenopathy was obtained in the second patient, a man aged 50, who was given mannomustine to a total of 700 mg. in the first course, the remission lasting only nine weeks; the glands have again regressed following treatment with a further 700 mg. A transient thrombocytopenia occurred after both courses of treatment.

Multiple Myeloma (1 case)

Complete relief of bone pain, regression of hepatomegaly and splenomegaly, a slight fall of the raised serum globulin level, and a fall to normal of the sedimentation rate have occurred after a total dose of 1,000 mg. of mannomustine given to one patient. The *x*-ray appearances of numerous skeletal deposits have not changed, but the marked symptomatic improvement has been maintained for three months.

Carcinoma (5 Cases)

Five patients suffering from advanced carcinoma have been given mannomustine. The total dose has ranged from 700 to 1,100 mg. Three patients had bronchial carcinoma with multiple secondary deposits, one patient had carcinoma of the stomach with secondary deposits in the liver, and one had a carcinoma of the breast with multiple secondaries elsewhere.

In one patient with a malignant pleural effusion, the mannomustine was given intrapleurally, as much as 500 mg. being injected at one time, without any immediate local or general adverse effects.

Beneficial effects were slight; temporary regression of secondary deposits in lymph nodes was noted in two patients, and relief of pain for a period of three weeks was obtained in two others, but there was no effect on the primary growth or on any liver or secondary skin deposits. Anaemia developed in all patients within six weeks; a severe neutropenia occurred in two patients and thrombocytopenia in two others, resulting in death from gastro-intestinal haemorrhage in one of them.

All five patients died within eight weeks of beginning treatment with mannomustine.

Polycythaemia (4 cases)

The effect of treatment with mannomustine in four cases of polycythaemia is shown in Table IV. The mannomustine was given in doses of 100 mg. on alternate days until the total amount had been given.

Beneficial effects were obtained in all the patients, and in three of them (Cases 32, 34, and 35) the remissions were continuing after six, four, and three months respectively. Case 33 required a further short course of mannomustine after six weeks. One patient (Case 32) suffered from severe pruritus, which had failed to respond to all previous treatments, but complete relief of this symptom followed mannomustine therapy. The spleen was enlarged in Cases 34 and 35 and became impalpable after treatment. A transient leucopenia occurred in two patients after six weeks, and there was a symptomless transient thrombocytopenia in three patients after three to five weeks.

Toxic Reactions

Gastro-intestinal.—Of the 45 patients treated with mannomustine, 19 (42.2%) had some gastro-intestinal side-effects—anorexia, nausea, or vomiting At some time during the course of treatment 41 patients were given individual doses of 100 mg. (1.5–2.5 mg./kg.): mild anorexia and nausea occurred in 13 (31.7%) and vomiting in 6 (14.6%). Doses greater than 100 mg. were usually associated with severe nausea and vomiting. In 17 patients individual doses of 150–500 mg. were given. Of these, 5 (29.4%) had no gastro-intestinal side-effects, one patient receiving two injections of 500 mg. each on alternate days. Nausea and malaise began three to six hours after the injection and lasted for between 4 and 36 hours. When patients were treated on alternate days they had normally recovered before the next injection. Rarely, toxic symptoms would last for two to three days. In those patients who complained of nausea and vomiting, a decrease in symptoms following the use of 1,000 mg. of ascorbic acid in aqueous solution as a solvent, in place of physiological saline, was noted in some patients, and the simultaneous use of chlorpromazine (25 mg. four times daily) often resulted in further reduction or relief of symptoms. Intrapleural injections of 50–500 mg. have been given without ill effects.

Local Reactions.—In three patients a small volume of the mannomustine solution accidentally leaked into the extravascular tissues. The patients complained of severe pain at the injection site within three to four hours, and each developed an extremely tender, erythematous, indurated mass which slowly enlarged over a period of two to three weeks. The mass was still present four to five months later.

Bone Marrow.—Table V shows the frequency with which the severe but mostly transient depression of bone-marrow function occurred after mannomustine therapy. The thrombocytopenia developed within four to five weeks and leucopenia within five to six weeks after the beginning of treatment; both were usually symptomless and lasted two to three weeks only. Granulocytes and lymphocytes were depressed equally in most cases, only one patient developing a temporary agranulocytosis. Two patients with Hodgkin's disease (Cases 23 and 26) who were each given a second course of mannomustine three months and four months later, respectively, again developed marrow depression, which has lasted two to three months and has failed to improve with steroid therapy. Anaemia, developing six to eight weeks after treatment, was particularly frequent in the patients with reticuloses or malignant disease. In the patients with a reticulosis, the haemoglobin had usually returned to near pre-treatment level within six weeks, but two developed persistent aplastic anaemia after the second course of treatment. In four patients the principal cause of death was aplastic anaemia or haemorrhage from thrombocytopenia. They were, however, in the terminal stage of their illness. Prednisolone did not appear to facilitate marrow recovery.

TABLE V.—*Toxic Effects on Bone Marrow Following Treatment With Mannomustine (Excluding Acute Leukaemias)*

Diagnosis	No. of Patients	Anaemia	Leucopenia	Thrombocytopenia
Chronic myeloid leukaemia	12	—	1	1
" lymphatic "	3	—	—	1
Hodgkin's disease	10	6	5	5
Brill–Symmers disease	2	1	1	1
Reticulosarcoma	2	1	1	2
Myeloma	1	—	1	1
Carcinoma	5	5	2	2
Polycythaemia	4	—	2	3
Total	39	13 (33%)	13 (33%)	16 (41%)

Discussion

In this series of cases the percentage with gastro-intestinal side-effects (42.2%) after doses of 1.5 to 2 mg./kg. was similar to that reported by Sellei and Eckhardt (1958). When doses of 3 to 7 mg./kg. were given the percentage increased considerably (70.6%). Like Szentkláray (1958), we observed some reduction of these side-effects when the drug was dissolved in ascorbic acid solution instead of physiological saline. Concurrent administration of chlorpromazine was of value in some patients. Sellei and Eckhardt, from the results in their series of cases treated with mannomustine over a period of two years, consider the drug to be superior to other chemotherapeutic agents in chronic lymphocytic

TABLE IV.—*Effect of Mannomustine in Polycythaemia Vera*

Case No.	Age and Sex	Before Treatment					Total Dose mg. (mg./kg.)	After Treatment					Duration of Response (Months)
		R.B.C. 10^6/c.mm.	Hb g./100 ml.	P.C.V. %	W.B.C. 10^3/c.mm.	Plts. 10^3/c.mm.		R.B.C. 10^6/c.mm.	Hb g./100 ml.	P.C.V. %	W.B.C. 10^3/c.mm.	Plts. 10^3/c.mm.	
32	75 F	6·73	16·4	—	34	545	800 (18·2)	4·22	11·1	—	2·3	51	6
33	54 M	6·32	13·0	—	5·1	204	500 (5·5)	5·9	10·5	—	No change	No change	1·5
34	64 M	8·98	16·6	72	25	562	800 (11·0)	5·4	15·5	35	5·4	37	4
35	47 M	8·72	23·6	76	10	270	900 (13·6)	5·6	17·0	47	2·4	51	3

leukaemia and equal to other drugs in chronic myeloid leukaemia. They stressed the value of combined treatment with mannomustine and busulphan or demecolcine in chronic myeloid leukaemia, but did not state in how many cases this combined therapy was used. They also reported favourable results in Hodgkin's disease, other reticuloses, and multiple myeloma.

Our results in chronic myeloid leukaemia were disappointing. A satisfactory response was obtained in only two patients, both of whom shortly relapsed. In the remaining 10 patients control was inadequate and of very short duration, apart from one patient with an extremely sensitive bone marrow, the white-cell count remaining under 25,000/c.mm. for over eight months. The responses to further courses of mannomustine given to six patients were even less satisfactory than those following the initial courses.

That mannomustine may be effective in cases resistant to other chemotherapeutic agents is illustrated by one patient (Case 11) who had become resistant to busulphan and failed to respond to intravenous nitrogen mustard (trillekamin). A satisfactory reduction in the white-cell count was achieved with mannomustine; it was unfortunately of short duration, and the patient refused further injections because of very severe nausea and vomiting.

Apart from the generally unsatisfactory response of chronic myeloid leukaemia to mannomustine therapy, the practical difficulties of administering daily or alternate daily intravenous injections to out-patients who may have to travel considerable distances to attend the clinic makes the drug very much inferior to busulphan, which is undoubtedly the drug of choice (Galton and Till, 1955; Wilkinson, 1955a, 1955b).

Although three is too small a number of cases to assess adequately the value of a drug, our patients with chronic lymphocytic leukaemia have illustrated the considerable variation in response that can be obtained. The responses in further patients treated with mannomustine will have to be very much better if the drug is to compare favourably with trillekamin (Wilkinson, 1953, 1955a, 1955b) or chlorambucil (Galton *et al.*, 1955).

Mannomustine would appear to be of some value in Hodgkin's disease, good responses being obtained with five patients and moderately good ones with four others. The responses, however, were not as good as have been achieved with trillekamin; many more injections were required, and they produced more toxic effects generally and on the bone marrow than are obtained with trillekamin (Wilkinson, 1955a, 1955b). Mannomustine would appear to be more effective than thiotepa in Hodgkin's disease, as complete regressions of hepatomegaly, splenomegaly, and mediastinal lymphadenopathy have been obtained in most cases, whereas thiotepa is relatively inactive in Hodgkin's disease involving these structures (Leonard *et al.*, 1956). Toxic effects on the bone marrow, however, were much more marked than with thiotepa.

Two cases of Brill–Symmers disease and one of reticulosarcoma benefited from treatment, and the patient with multiple myeloma showed such good symptomatic and some objective improvement that it will be worth while treating further cases either with mannomustine alone or in combination with urethane. Mannomustine was of little value in the five cases of carcinoma: indeed, the severe anaemia and the thrombocytopenia produced in two cases may well have contributed in some degree to their more rapid deterioration.

Satisfactory remissions have been obtained in three patients with polycythaemia vera, while the fourth patient, who was initially given a small total dose, is now responding satisfactorily to a second course of mannomustine. It is not yet known whether remissions of comparable length to those obtained using other agents such as thiotepa (Leonard *et al.*, 1956) will occur, but mannomustine may prove to be another useful method of treatment.

In addition to the reduction of the occasionally observed high white-cell count in some acute leukaemias, the simultaneous symptomatic improvement that was also obtained would appear to support the careful use of mannomustine in such types of case.

Disadvantages of mannomustine treatment in diseases other than chronic myeloid leukaemia are (*a*) the potentially serious although usually transient bone-marrow depression, especially if a second course is given within four months of the first; (*b*) in many cases there may be undesirable gastro-intestinal side-effects; and (*c*) occasional painful local effects.

This bone-marrow depression does not appear to respond to prednisolone.

Summary

A new cytostatic compound mannomustine (1 : 6-bis(β-chloroethylamino) - 1 : 6 - deoxy - D - mannitol dihydrochloride) has been used in the treatment of 45 patients with leukaemias, polycythaemia, reticulosis, and malignant disease.

A dosage schedule of 100 mg. daily or on alternate days to the required total amount is the most satisfactory.

It was not found to be as efficient as the present accepted agents such as trillekamin, busulphan, or demecolcine for the treatment of chronic myeloid leukaemia

Mannomustine is of some value in the treatment of chronic lymphatic leukaemia, Hodgkin's disease, Brill–Symmers disease, reticulosarcoma, multiple myeloma, and polycythaemia.

Pain may be relieved in carcinoma, but severe bone-marrow depression may occur.

Mannomustine may be of value in the treatment of acute leukaemia, particularly the monocytic type, if the initial white-cell count is much increased.

Toxic effects can be severe, particularly on the bone marrow and especially if a second course has been given within four months; gastro-intestinal side-effects, nausea, or vomiting occur in 42% of patients after single doses of 1.5–2 mg./kg., but as high as 70% after doses of 3–7 mg./kg.

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COMMUNITY NEEDS OF ELDERLY PSYCHIATRIC PATIENTS*

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Treatment and care of psychiatric patients within the community rather than in the overcrowded wards of mental hospitals have been recommended by a Royal Commission (Report, 1957) and are about to become one of the corner-stones of the new Act of Parliament governing the legal aspects of mental illness. Recent accounts of out-patient, day-hospital, and domiciliary psychiatric treatments have gained so much attention that it is unnecessary to summarize them here.

Few people would deny that these movements are in the right direction and are likely to benefit a large proportion of patients. But, to avoid imposing undue strain on their families, treatment of psychiatric patients within the community will have to be conducted in a spirit of flexibility and co-operation between hospital and community. We cannot overstress the paramount need for rapid and, if necessary, repeated interchanges between specialist treatment under the aegis of the hospital, and aftercare and support by the family, the general practitioner, and the services of the local authorities. Co-operation in passing the ball rather than the buck is a *conditio sine qua non* if patients who are both mentally disordered and elderly are to be treated outside hospitals; and workers like Macmillan (1957) and DeLargy (1957) have pointed the way in which rapid changes between specialist treatment and community care can be achieved. Hospital costs can no doubt be greatly reduced by cutting down the time spent by people occupying hospital beds, but the public should be warned that adequate community services for the discharged patient are likely to be very expensive in terms of man-power (general practitioner and specialist time, home nursing, occupational and social therapy, etc.), of buildings, and of transport from home to treatment and occupation centres.

We would like to submit the results of an investigation designed to assess the amount of further help needed by a group of discharged elderly psychiatric patients.

Design of Investigation

All 131 patients discharged from the geriatric unit of our hospital during 1955 were followed up over the 24 months after leaving in-patient care. In some cases we were in possession of all relevant facts by reason of continued personal contact over this period; in others information was obtained by psychiatric social work or correspondence with hospitals. No patient was lost from this inquiry, but six cases were omitted from the analysis of our data because information was incomplete. We were able to assess the amount of further treatment our patients had received, and also to pick up cases who, though showing psychiatric symptoms, had not received further attention from psychiatry during the whole or part of the two years under review, and who therefore might be deemed to have been in need of help from the community. Implicit in this line of reasoning is the assumption that the community could have done one of two things for these old people: (1) supported them in such a way as to make specialist treatment unnecessary, or (2) guided them towards early resumption of psychiatric treatment.

In this study we were concerned only with finding out the proportion of patients requiring further treatment, the numbers needing community care, and the length of time during which community action was needed. We have not attempted a critical evaluation of the assistance our patients received or failed to receive, but, before coming down to an analysis of our data in a statistical fashion, it might be of interest to have a short account of the impressions we have gained during our follow-up study.

Impressions of Community Aftercare

In many areas south of the Thames, from which most of our patients came, the usual services for the elderly, such as home helps, Meals on Wheels, old people's clubs, etc., are provided. But they are limited by lack of money and man-power. Meals on Wheels service, for example, is a valuable aid; but it often functions only three times a week, or dinners for two days are left at one time. Probably this works well with old people interested in food, but it is well known that many old people with residual mental symptoms need to be coaxed to eat, and the mere fact that someone comes to the door every day, plate in hand, says an encouraging word, and perhaps helps to find a knife and fork, may mean the difference between a meal eaten and one left to congeal on the table.

Another service of which far more is needed is the Incontinent Laundry Collection. We recall, from our group, one old man enabled to keep his demented wife out of hospital for much longer than had been anticipated with the help of this service. In fact, two hospital beds were kept free in this case, because it was not long after the wife had to be removed to hospital that the husband, possibly because he had been deprived of having to minister to his wife's needs, followed her there.

Home-help services seem to be of more use to women than to old men living alone, who often have an aversion to letting strange women into their abodes. Even so, there were several men who stayed out of hospital or Part III accommodation for lengthy periods because they were provided with a varied range of domestic services by the local authority or voluntary bodies.

Friendly visiting is particularly valuable in the after-care of elderly patients, provided it is done regularly. Unfortunately, this appears to be available in only few areas. One woman in our group seemed to need the stimulus of almost daily visiting to maintain contact with the outside world of reality. This we could not obtain for her, and she withdrew into herself, failed to go out to buy food, and very soon relapsed into the persecuted behaviour which had led to her admission; long-term care in a mental hospital finally became necessary. In addition to stimulating and encouraging the ex-patients, there are some chores which can easily be done for them by a regular visitor. He or she will not only bring life into the home, but can also become an ally for shopping expeditions or changing of library books, and so prevent the old person from becoming house-bound for

*Based on a paper read at the 1958 Autumn Meeting of the Royal Medico-Psychological Association.

psychological reasons. On the other hand, we must not overlook the fact that some of our patients remained unreceptive to efforts of socializing them in this fashion.

Quite a number of our patients successfully returned to their pre-illness occupations, and it has been our experience that if a patient was really fit on discharge he would, if he so desired, find employment by himself; if he did not much wish to work the combined efforts of disablement resettlement officer and psychiatric social worker tended to fail. In times of partial unemployment more strenuous efforts will have to be directed towards making the public realize that part-time work may result in a significant contribution to the mental health of our increasing elderly population.

It may be impossible to ascertain whether a patient, while he is living in hospital, is fit for the stresses of the outside world, including employment. We have felt the lack of halfway-houses where the patient's ability to tolerate the outside world might have been assessed, and from whence the elderly person, in order to gain the independence which a salary gives, might be launched into a job suited to his present capabilities. Halfway-houses would have been useful also to housewives and retired people whose adjustment to the outside world still seemed precarious. We discovered that several of the patients, who had left us for various homes, eventually improved enough to face returning to their own abodes.

We were often discouraged by the small amount of aftercare likely to be available in some of the areas to which our patients were discharged on account of the inadequate establishment of trained social workers. In this connexion it is of great interest that only one of a number of our ex-patients with whom the P.S.W. had been able to keep up regular contact had to be readmitted during the period under review. One severely persecuted patient was kept out of hospital largely through the persevering care of her local old people's welfare secretary, who often consulted the P.S.W. On the other hand, there were, unfortunately, patients who were unable to use services that were offered to them; they tended to fall into two groups. There were those who remained too ill to benefit from P.S.W. contact, though not so severely disordered in behaviour to require in-patient care—for example, one elderly man whom the P.S.W., in spite of active support from the patient's wife, herself an ex-mental nurse, was unable to mobilize towards a club and other facilities only a stone's throw from his house. Secondly, there were the people who "always kept themselves to themselves," and who resisted attempts at socialization. But frequently in these cases, and in others, members of the patients' families appeared to benefit from occasional opportunities of blowing off steam and of having a sympathetic listener in the social worker.

We have been unable to assess the amount of help our patients had been receiving from their family doctors, though many patients had consulted them. But without putting the G.P.s to great trouble it would not have been possible to find out what proportion of these contacts had been for psychiatric complaints. There were a number of instances where we had evidence for much active support from the family doctor, but it was rare for him to establish contact on his own initiative with a patient of whose discharge he had been notified by letter. Patients often alleged—and one should perhaps not put too much trust in these statements—that their G.P.s had said that they were now "under the hospital."

Characteristics of Sample

All patients had been admitted on a voluntary basis and had reached the unit via the out-patient department of the hospital, its domiciliary service, a mental observation ward, or after recommendation by psychiatrists not on the hospital staff. Only patients suffering from deterioration over long periods and finally requiring long-term care were not accepted. We are therefore dealing with a sample from which cases with the worst prognosis had been excluded.

There were 49 men and 76 women, between the ages of 60 and 84, with the majority over 70 years old. A diagnostic breakdown is given in Table I, and the predominance of affective (mainly depressive and anxious-agitated) symptomatology in this sample emerges clearly.

TABLE I.—*Diagnostic Breakdown of the 125 Patients*

Psychoses due to cerebral causes	36
Affective psychoses	56
,, illnesses with neurotic admixtures ..	20
"Paraphrenic" illnesses	13

An attempt has been made to separate off patients with severe affective disturbances and delusional elaborations of guilt or hypochondriacal thought content from those with milder affective illnesses of neurotic severity. "Paraphrenic" was used as a provisional label for patients whose persecutory or schizophreniform symptoms were not associated with obvious affective or psycho-organic features.

Community Needs of Members of Sample

Early Treatment Aspects

Hospital services as constituted at present are limited to the treatment of actual illness. Prevention and aftercare are in the hands of family doctors and the medical services of local authorities. Prevention of psychological disorders in old age has not yet become a practical possibility, but much suffering of both patients and their families can be prevented by instituting treatment early in the illness.

In 93 of our patients admission to the unit had been the first attempt at treating the present illness, but in 74 cases symptoms had already been present for more than six months; 31 had been ill for more than two years. In view of the relatively poor response to specialist treatment of the paranoid illnesses and the neurotic depressions of the elderly, the long time-lag between inception of symptoms and hospital admission which we found in these groups may not be of much practical importance, but it is surely disquieting that of the 41 patients with affective psychoses—conditions which are well known to respond promptly to modern forms of treatment in a large proportion of cases—only 8 were referred for treatment during the first six months of their illnesses, while 17 had been ill for well over one year before receiving psychiatric attention.

These figures need not be interpreted as signifying that patients and their families were slow in seeking medical advice, or that the family doctors had been dilatory in referring elderly patients to psychiatrists. It is generally accepted that the management of affective illnesses presents a large item of the G.P.'s work (Watts, 1957), and it may well be that the patients who reached us so late in their illness represented the small proportion of cases in which his treatment had failed. On the other hand, there were several instances where the true nature of the illness had not been recognized for some time.

It has been shown (Cosin *et al.*, 1958) that treatment of established dementing disorders in old people produces only very modest responses, and that in these conditions therapeutic results are unlikely to improve unless early treatment can be instituted. In our present material there had been a long time-lag between the date around which the appearance of organic mental symptoms was retrospectively recalled by relatives and admission. Of 33 cases, 24 had been deteriorating for at least one year, and 18 for over two years. This is yet another reminder to those responsible for the elderly of the community that they will have to consider urgently efficient ways of discovering early cases of senile mental decline and methods to attempt prevention of further deterioration.

Aftercare Needs

Aftercare needs have to be assessed against the background of the patients' clinical state during the two years following discharge from hospital, which is given in Table II. Two patients with organic mental disorders had been discharged by death, and our number has therefore been reduced to 123. Our patients had been in hospital for periods averaging three and a half months, and all but the few who left against advice had been sent out only after it was felt that no further psychological, physical, or environmental therapy was likely to produce further improvement. It will be seen that in spite of thorough treatment only 15% made complete and lasting recoveries, while a further 22% recovered

TABLE II.—*Clinical State During the Two Years Following Discharge*

	Organic Psychotics	"Psychotic" Affectives	"Neurotic" Affectives	"Paraphrenics"	All Diagnoses
Completely symptom-free throughout ..	2	12	4	1	19
Intermittent or continuous mild symptoms	5	11	8	5	29
Intermittently disabled ..	2	19	4	2	27
Continuously disabled ..	25	14	4	5	48
Total ..	34	56	20	13	123

but had early recurrences: 24% of ex-patients continued to be subject to mild symptoms, and 39% remained continuously disabled by severe symptoms. As one might expect, results of treatment had been most disappointing in patients with mental symptoms due to cerebral deterioration or disease, but failure to recover from affective disorders and the high incidence of early recurrences in these conditions also emerge very clearly.

These findings underline the fact that psychiatric disorders, like most illnesses in old age, tend to become chronic or recurrent, and, in keeping with this, our follow-up investigation showed that only 29% of patients did not receive any further psychiatric attention apart from one or two routine follow-up checks in the out-patient department or by P.S.W. visit; 20% had received further out-patient department support from our clinic; 31% had both in- and out-patient treatment at our or other psychiatric hospitals; and 20% had required further in-patient treatment (Table III). This outcome was particularly common in the organic group, where it usually meant long-term care. Further in- and out-patient treatment was given most often in the "psychotic" affective group, in keeping with the high recurrence rate of this disorder.

TABLE III.—*Treatment Given During the Two Years Following Discharge*

	Organic Psychotics	"Psychotic" Affectives	"Neurotic" Affectives	"Paraphrenics"	All Diagnoses
No treatment apart from follow-up attendances	9	12	11	4	36
Out-patient support only ..	5	13	3	3	24
Further out-patient and in-patient treatment ..	7	25	5	2	39
Further in-patient treatment only	13	6	1	4	24
	34	56	20	13	123

Thirty patients had further treatment for more than 18 months, 39 for 6 to 18 months, and 18 for less than 6 of the 24 months under review. The amounts of time spent under specialist care would have been even greater had it not been for the fact that 23 of the 123 ex-patients died during the follow-up period. All but one had had continuously severe symptoms—in the majority, of the organic mental reaction type.

We have at last reached the point where we may attempt to assess the amount of community care which our sample of elderly psychiatric patients required after discharge. Though we have just seen that these patients had received a good deal of further specialist attention at our hospital and at other centres, scrutiny of our data showed clearly that many of them had received no psychiatric treatment at all in spite of continued mental ill-health, or that they were left without specialist help for prolonged periods. By subtracting the number of months during which patients had been receiving psychiatric care from the number of months throughout

TABLE IV.—*Number of Months During Which Patients Needed Community Help (That is, During Which They were Ill, but not Receiving Psychiatric Treatment)*

	Organic Psychotics					"Psychotic" Affectives					"Neurotic" Affectives					"Paraphrenics"					All Diagnoses					Total
	Mths. Ill Without Psychiatric Treatment					Mths. Ill Without Psychiatric Treatment					Mths. Ill Without Psychiatric Treatment					Mths. Ill Without Psychiatric Treatment					Mths. Ill Without Psychiatric Treatment					
	0	<6	6<12	12<18	18<24	0	<6	6<12	12<18	18<24	0	<6	6<12	12<18	18<24	<6	<	6<12	12<18	18<24	0	<6	6<12	12<18	18<24	
Completely symptom-free throughout ..	2					12					4					1					19					19
Intermittent or continuous mild symptoms ..	1	1	2	1		6	1		1	3	2			2	4	3				2	12	2	2	4	9	29
Intermittently disabled ..	1		1			17		1	1		3		1			2					23		3	1		27
Continuously "	14	1	2	4	4	10		2	1	1	1			2	1	3		1	1		28	1	5	8	6	48
	18	2	5	5	4	45	1	3	3	4	10		1	4	5	9		1	1	2	82	3	10	13	15	
	34					56					20					13					123					

which they were suffering from symptoms, we were able to obtain, as the difference, the periods of time during which some help from the community, including the family doctor, had been desirable. Many of these patients had, in fact, been supported by agencies of the community or had finally been referred back for psychiatric treatment, as discussed in an earlier section of this paper. Here we are concerned only with showing the number of months during which patients had been in need of some form of community action, because on the one hand they had been unwell, but, on the other, had not been receiving psychiatric help. As we are dealing here with the main subject of this communication our complete data are presented in Table IV.

Subjects have been tabulated by (1) original diagnosis and (2) clinical status during the follow-up period independently of diagnosis, against the number of months during which they were suffering from psychiatric symptoms, but not under specialist care, and thus presumably in need of community action. For the sake of completeness we have included those ex-patients who had remained mentally well and had needed no help. Taking a superficial view, there were 82 people in whose cases community agencies would not have contributed towards better care, because they had remained well throughout the two years under review, or because they had been receiving treatment promptly on recurrence of symptoms or had been safely in hospital for long periods. But we have been unable to assess what proportion of these long-term hospital patients did in fact have unsatisfied needs of community care, in that they should have been transferred from mental hospitals to residential accommodation or domiciliary care provided by voluntary organizations or local authorities.

Forty-one patients, exactly one-third of all cases, without any doubt went through periods during which action by the community might either have been therapeutic or should have brought people back into psychiatric treatment at an earlier date; in 15, community needs had been present throughout the whole of the two years under review, and in 26 during shorter periods. We may also see from Table IV that the needs of the patients with recurrent attacks and intervening periods of reasonably good mental health were minimal, but that 20 of the 48 continuously disabled patients may not have been under any form of psychiatric treatment or supervision for lengthy periods while they and their families were clearly in need of help. The majority of old people with mild symptoms were in the same position for many months, which is an even more important finding, because these mild disorders should respond to community care so much better than severe illnesses or dementias.

Looking at openings for community action in terms of the various diagnostic categories, we found that the needs of the organic psychotics were greatest; next came people with affective disorders on a neurotic background. But even the needs of patients with psychotic affective illnesses arising more often in stabler personalities were by no means negligible in our age group (11 of the 44 not continuously well). We know from clinical experience that paranoid old people often respond, at any rate for a time, to simple common-sense measures without psychiatric advice.

Summary and Conclusions

Our findings demonstrate that, in the fields of prevention and early treatment as well as that of after-care, the scope for community action in the case of elderly psychiatric patients is frighteningly large. In our experience with one year's discharges from a unit for recoverable cases over the age of 60, only 15% of patients remained completely well over the next two years, and 71% received further psychiatric treatment. Of the 104 patients with recurrent or continuous symptoms, at least 41 (39%) had been in need of community action coming from the family doctor, voluntary organizations, or services run by the local authority. We also recorded our impressions of the community care which was in fact given to this sample of patients, but obviously failures had come to our attention more often than successes.

Both general impressions and our statistics point to the same conclusion: any worth-while community service for elderly people with psychological illnesses or difficulties will have to cater for very large numbers, and will turn out to be very expensive in terms of man-power and money. At the same time, beyond vague impressions, very little is known about the therapeutic effectiveness of community care in this group of psychiatric conditions, and we venture to suggest that any future community programmes for elderly people be introduced step by step and in accordance with plans which will allow of scientifically conducted and controlled assessments of the value of community care of elderly psychiatric patients.

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LONG-TERM ANTICOAGULANT TREATMENT OF CORONARY THROMBOSIS IN GENERAL PRACTICE

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Anticoagulant therapy in the early stages of coronary thrombosis is now generally acknowledged to be beneficial and is widely practised. Long-term treatment with anticoagulants is much less extensively used, though Tulloch and Wright (1954) started giving it in 1940, and up to 1952 had treated 227 patients for periods of up to eight years.

Short-term anticoagulant therapy is the use of anti-coagulants during the first three to four weeks of the illness. Long-term therapy is treatment carried on for longer than four weeks, either immediately after the onset of the illness or at any subsequent time.

The literature is liberally studded with articles on long-term anticoagulant treatment in hospital out-patient departments and in consultant private practice (Foley and Wright, 1949; Hines and Barker, 1949; Cosgriff, 1950; Bay *et al.*, 1954; Borg, 1956; Breddin, 1957; Estes, 1957; to name but a few). In sharp contrast I have been able to find only one article (Putnam, 1957) which describes the experience of a general practitioner

in this form of therapy, and that was in the U.S.A. General practitioners therefore do not use long-term anticoagulants, or are remarkably reticent about their results.

The experience of a general practitioner in giving long-term anticoagulant therapy in an urban and rural practice might therefore be of interest and give encouragement to other general practitioners similarly placed.

At the time of writing 12 patients (10 males, 2 females) have been under treatment; one for 32 months, one for 18 months, four for 12 months, one for 8 months, one for 7 months, one for 5 months, two for 4 months, and one for 3 months. The accompanying Table gives the weekly prothrombin values. The number

Weekly Prothrombin Values (%) in 12 Patients under Treatment During the Past Year

Week	1	2	3	4	5	6	7	8	9	10	11	12
1	30	30	17		30	50		21	14			
2	13	27	13		30	27		33	30			
3	17	36	13		19	30		—	19			
4	18	33	18		45	30		—	18			
5	13	27	15		50	50		40	17			
6	12	27	22		36	45		19	22			
7	27	27	20		45	40		19	21			
8	17	18	19		21	25		‡	14			
9	18	27	36		15	36		‡	19			
10	17	25	14		19	45		‡	16			
11	17	40	90		22	45		‡	16			
12	17	30	21		20	25		20	18			
13	19	27	30		30	18	30	18	17	33		
14	19	23	40		23	17	20	14	14	25		
15	21	30	22		33	23	50	18	21	30		
16	17	30	19		30	21	18	19	—	33		
17	21	33	70		30	27	19	21	20	33		
18	23	22	30		22	21	16	30	17	36		
19	30	30	40		20	23	25	25	33	20		
20	36	23	45		23	36	23	55	50	25		
21	30	40	27		13	33	40	33	25	33		
22	30	30	40		23	45	28	33	25	28		
23	30	36	30		17	22	26	—	13	34		
24	45	50	36		20	23	27	33	55	45		
25	33	21	40		30	30	25	33	21	50		
26	55	33	45		21	30	20	45	36	40		
27	50	*27	20		30	30	27	—	27	55		
28	45	100	27		17	27	21	27	45	40		
29	22	100	< 10		19	—	25	50	27	†		
30	16	100	90	40	18	33	17	55	22			
31	21	†	50	30	30	45	50	45	33			
32	45		55	21	50	36	33	33	36			
33	25		18	23	55	40	45	21	45			
34	22		21	15	22	27	33	27	23			
35	23		23	55	19	21	23	40	23		70	
36	22		17	21	27	30	33	30	33		45	90
37	23		19	21	30	27	45	—	30		40	25
38	16		21	22	18	22	20	19	18		30	18
39	19		25	27	40	21	*19	—	17		36	20
40	27		17	25	19	33	23	50	30		70	14
41	—		22	18	—	55	25	25	20		—	—
42	27		23	18	—	27	20	16	20		38	—
43	20		20	25	20	23	45	22	22		27	17
44	33			36	30	36	55	23	—		36	13
45	55		21	55	30	33	23	27	22		50	27
46	18		20	18	20	20	55	—	22		17	50
47	50		21	25	25	36	†	18	19		36	22
48	45		18	21	22	23		18	20		40	21
49	30		19	23	19	40		—	19		30	19
50	36		19	25	40	27		19	25		45	25
51	21		22	18	17	27		23	21		19	25
52	30		30	25	30	27		45	20		21	20

* Dosage reduced with a view to stopping treatment.
† Treatment stopped on account of duodenal ulcer.
‡ In hospital with mild cardiac failure.

concerned is too small for the results to have any statistical value. Most of the men were in their forties or early fifties, and had been admitted to hospital as soon as the coronary infarction had been diagnosed clinically and confirmed by E.C.G. There they were all treated with anticoagulants, and this therapy was continued when they returned home.

The usual procedure is as follows. When notification is received that the patient has returned home, the type and dose of the anticoagulant is ascertained from the physician in charge of the case at hospital, the patient is visited, and the appropriate drug prescribed. Next day, before the morning surgery, the patient is visited again and a sample of blood taken for prothrombin estimation. This is then dispatched by bus to the laboratory so that the test can be carried out before the blood is more than a few hours old. The laboratory telephones the result in the afternoon. If this is satisfactory the test is not repeated for a week; if unsatisfactory, an appropriate adjustment is made in the dosage (the patient's relatives are instructed to communicate with the surgery, by either telephone or messenger, at about 6 p.m.) and the prothrombin test is repeated in two or three days until a fairly steady level (about 20%) is achieved. It is then done only once weekly unless wide fluctuations occur. If stability is not reached reasonably soon a different drug is tried. After four to five weeks the patient is usually well enough to attend the surgery once weekly to have his blood taken, but sometimes he may require to be visited weekly for 8 to 12 weeks.

Indications and Contraindications

At most centres long-term anticoagulant treatment is reserved for the more seriously ill cases. Estes (1957) recommends it only when (1) there is recurrence of infarction with short free intervals, (2) there are recurrent thrombo-embolic complications following coronary infarction, and (3) there is cardiac failure or certain types of arrhythmia. Breddin (1957) reserves it for all cases of second and subsequent infarctions, diabetics, those with marked lipaemia, those with severe angina, and all women on account of the high mortality in females. Tanzi and Van Ness (1947) give it only to poor-risk patients who have any one or a combination of the following: previous myocardial infarction, intractable pain, extreme or persistent shock, much-enlarged heart, gallop rhythm, congestive heart failure, auricular flutter or fibrillation, ventricular tachycardia or intraventricular block, diabetic acidosis, obesity, previous pulmonary embolism, varicose veins, or past or present thrombophlebitis. Borg (1956) recommends it in impending cardiac infarction. Toohey (1958) excludes those who have only a moderately severe attack or a first attack.

In the present series I have accepted rather different indications. Though three of the cases had at least two infarcts before long-term treatment was started, the aim was to keep even the first-timers from getting a further attack and so enable comparatively young and otherwise fit men to continue to carry their business and family responsibilities. In other words, the indications were as much economic as medical.

Selected patients must be intelligent enough to understand the nature of their illness and of the treatment, and they must be made aware of and accept the risks inherent in the latter. They must also be in such an occupation that, when they resume work, they will be able to attend morning surgery at least one day a week for prothrombin control.

Contraindications.—These have been detailed by previous authors, especially Estes (1957). They may be summarized as follows: anticoagulants should not be given (1) in any condition tending to cause haemorrhage—for example, purpura; active peptic ulcer; gastric, colonic, or bladder carcinoma; oesophageal varices; haemorrhoids; and, probably, recent cerebral thrombosis; (2) in impaired hepatic or renal function; (3) where the patient is not sufficiently dependable or co-operative in regard to taking the proper dosage of the drug, or in attending as directed for blood tests and

the results of same; and (4) where the patient is not intelligent enough to carry out emergency treatment for himself if haemorrhage should occur.

Difficulties in General Practice

The chief difficulty is the transport of blood samples to the laboratory in time for testing on the day they are taken. The postal service is of course too slow. For the first 12 months they were taken by private car, later by public bus service. Because of transport difficulties the samples occasionally failed to arrive in time. As the laboratory will not carry out tests on specimens 24 hours old further samples had to be taken next day. Watson (1956) and Neilson and Briggs (1957) claim that a sufficiently accurate estimation can be made on specimens not more than 24 hours old, but Dr. C. R. Murdock, of the local laboratory, thinks that this is not so (personal communication). Recently, by courtesy of the local hospital committee, a satisfactory collection service has been arranged, and the samples travel up to the laboratory in the hospital box.

It would be difficult to carry out this treatment in a single-handed practice, as it is necessary for the satisfactory working of the scheme for someone capable of taking the blood and adjusting the dosage to be in attendance always at the appropriate times should one doctor be absent for any reason.

Precautions

Before treatment was started the patients were warned of the dangers inherent in the treatment and also of the possible dangers in stopping too abruptly. They were also told of the need for regular attendance for prothrombin tests and the necessity for ascertaining the result of the tests, together with any change of the dosage, on the same evening. All cases were blood-grouped by the courtesy and co-operation of the Northern Ireland Blood Transfusion Service. An extra page was stuck in the blood group cards stating: "I am receiving anticoagulants; my prothrombin is approximately 20%. In the event of haemorrhage or accident please call a doctor or consult my own doctor, Dr. ....., Tel. ....., as I may require an injection of vitamin K_1 (10 mg. of 'konakion' or 'mephyton')." I understand a similar card is supplied by the American Heart Association (*British Medical Journal*, 1958). In addition, each of our patients is provided with two 10-mg. gelatin capsules of phytomenadione (vitamin K_1) to take by mouth if he notices bleeding from any of the body orifices and warned to contact us immediately if this should occur.

Hospital treatment, including blood transfusion if required, should be available within reasonable distance. If the subject is likely to be out of reasonable distance from a hospital and/or testing laboratory—for example, holidaying abroad—it may be wise to reduce the dosage of anticoagulant by 5–10% below that which he ordinarily takes to keep him at optimum level, or, alternatively, he may reduce the dosage by 10–15% on one day a week in order to check any fall in the prothrombin level which may be occurring. The patients are also warned against certain drugs, especially acetylsalicylic acid, which, in addition to its irritant effect on the gastric mucosa, may also lower the prothrombin percentage. Bay *et al.* (1954) report that 4 g. of acetylsalicylic acid may prolong the prothrombin time to twice normal. Olwin and Koppel (1957) recommend that never more than 15 gr. (1 g.) of salicylates should be taken in one day. Phenylbutazone ("butazolidin") is contraindicated, as also are broad-spectrum antibiotics (Toohey, 1958). Marked alteration in the amount of alcohol imbibed daily may cause a fluctuation in the prothrombin level (Olwin and Koppel, 1957).

Any deficiency of vitamin C should be corrected and an adequate intake in the diet ensured (Wright *et al.*, 1954; Manchester, 1957).

Frequency of Tests

The recommended frequency of tests varies greatly. Jolly (1956) recommends intervals of 7 to 14 days. Olwin and Koppel (1957) say the period should never be longer than two weeks. Toohey (1958) controlled 105 out of 117 patients by testing only every 6 to 12 weeks. The other 12 patients were unstable but did not require testing more often than once in four weeks. However, he recommends more frequent tests during intercurrent illness. In the present series no patient went longer than eight days without testing unless on holidays, when other precautions, already described, were taken. This was because of sudden severe fluctuations, both upwards and downwards, which are partly due to the difficulty of accurately adjusting the dosage. It is very difficult to make a change of 2–3% in the daily dosage when that dosage is one tablet a day and only one strength of tablet is made—for example, "marcoumar."

Duration of Treatment

The duration of treatment recommended by different writers varies greatly. Estes (1957) suggests 6 to 12 months after the last thrombo-embolic episode; Breddin (1957) recommends one and a half to two years; Borg (1956) says two years at least, perhaps indefinitely. Askey and Cherry(1950) kept patients on it for two years. Foley and Wright (1949) and Suzman *et al.* (1955) suggest stopping after three years' freedom from symptoms. Tulloch and Wright (1954) have a few patients who have been under treatment for about eight years. Putnam (1957) has kept one patient on treatment for nine years.

It is proposed to continue with the present series indefinitely or until there is some indication for stopping. Treatment has been stopped in three cases. One patient is over 65 and had first a gastro-enterostomy for chronic duodenal ulcer and later a partial gastrectomy for stomal ulcer. He had three months' anticoagulant treatment. The other two patients were diagnosed radiographically as having duodenal ulcers after investigations for dyspepsia. They had seven and eight months' anti-coagulant therapy. Fortunately there were no overt haemorrhagic incidents in these patients with duodenal ulcers.

Discussion

Provided the laboratory facilities are reasonably close at hand long-term anticoagulant treatment by general practitioners for coronary thrombosis and related conditions is now a practical proposition. If it becomes universal the resulting increase in the number of tests to be done will place a heavy burden on the laboratory services, and some selection of cases will probably be necessary. This will pose many ethical problems. In America, where the patient must pay for services rendered, the cases will probably be selected automatically by the patients' means, and any extension of the laboratory services required will be financed automatically. Putnam (1957) states that one of the

causes of patients giving up long-term therapy in his series was that of expense and trouble. Under the National Health Service of Great Britain and Northern Ireland direct cost to the patient is not, of course, a selective factor. A heavy burden will also be thrown on the general practitioner, which was not envisaged when the capitation rate was struck, and it is a burden which will snowball as the years pass: the more successful the treatment the more patients will survive to require it.

Further, if the treatment is to be extended to every case which might benefit thereby as regards prolongation of life, regardless of age or capacity for work or ability to care for himself, the number of cases might be expected to increase threefold or fourfold, as not only would older cardiac infarcts become eligible, but also cases of intermittent claudication, pulmonary emboli, arterial embolism, recurrent thrombophlebitis, and auricular fibrillation. The latter might be included with advantage now in the case of younger people. Much increased laboratory facilities would therefore have to be provided. At present it is often a very difficult decision whether to start a particular case on long-term treatment, and, once started, whether to continue indefinitely. If further experience shows that it is almost as dangerous to stop long-term anticoagulants as never to begin, it will then be necessary to carry on indefinitely or until there is some strong indication for stopping.

While the present series is too small for any statistical conclusions, the results tend to agree with the favourable response reported by other writers. Ten men and two women had at least one attack of coronary infarction each in the past three years. No fresh attacks have occurred during anticoagulant treatment though three of the cases have had at least one relapse before beginning long-term anticoagulant therapy in a shorter period of time than they have been under treatment.

Summary

The many favourable reports on long-term anticoagulant therapy in coronary thrombosis coming from hospital and consultant practice are reviewed. Their multiplicity is in sharp contrast to the paucity of reports of similar treatment by general practitioners.

The experiences of a general practitioner in providing long-term anticoagulant therapy for 12 cases of proved coronary thrombosis are described. The period of treatment varied from 3 to 33 months and is still continuing. There had been no mortality at the time of writing. Indications, contraindications, precautions, and difficulties peculiar to general practice are outlined, and ethical and other problems in the selection of cases are discussed.

I am indebted to my partner, Dr. T. M. Hanna, my wife, Dr. Sandra Wylie, and Miss M. Gilmore for their practical and clerical assistance; to Dr. C. R. Murdock, the Central Laboratory Northern Ireland Hospitals' Authority, for doing the prothrombin tests; to the East Antrim Hospitals' Management Committee for its co-operation in the transportation of specimens; and to Dr. E. A. Cheeseman for his advice on statistics.

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MESENTERIC ADENITIS IN ASSOCIATION WITH ASCARIASIS

BY

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Hyperinfestation of the intestine with roundworms (*Ascaris lumbricoides*) is common in tropical climates and is due predominantly to low socio-economic and cultural levels. The clinical syndromes produced by hyperinfestation are many and varied, and the surgical complications of ascariasis, though perhaps less well known, include intestinal obstruction, perforation, and peritonitis, particularly in children (Ochsner *et al.*, 1949; de Silva, 1957).

In a case of intestinal obstruction due to roundworms it was noticed that the visceral peritoneum was lightly covered with a sticky yellowish fluid, and in five subsequent cases, the histories of which are given below, a similar fluid in the peritoneum was accompanied by hyperinfestation of the intestine with roundworms and well-marked mesenteric adenitis. This combination of lesions has not been described previously in the available literature.

Case 1

A boy aged 13 was admitted to hospital because of right-sided colicky abdominal pain of two days' duration. He had been treated for worms with Ayurvedic (native) medicines shortly after the onset of symptoms, but this had only increased the pain. He had not vomited, nor did he complain of nausea, but he had been constipated for three days. There were no other symptoms, nor had there been a history of similar attacks in the past.

On examination he was in good condition; his temperature was 98° F. (36.7° C.) and pulse rate 88 a minute. The lymph nodes were not enlarged. The abdomen was slightly distended, with guarding and marked tenderness in the right iliac fossa. There was tenderness also in the recto-vesical pouch on rectal examination. A

provisional diagnosis of appendicitis was made. At operation through a right paramedian incision a small quantity of sticky yellowish fluid was found in the peritoneal cavity. The appendix appeared normal, but there were between 60 and 75 roundworms in the lower ileum. The glands in the mesentery were enlarged, fleshy, oedematous, and pink. Appendicectomy was performed and a lypmh node taken for biopsy; the peritoneal fluid was also taken for bacteriological examination. The wound was closed without drainage.

His temperature was 100° F. (37.8° C.) on the day after operation; it fell by lysis to normal on the fifth day and thereafter remained normal. (No antibiotics were used.) A single dose of 1 oz. (30 g.) of piperazine citrate was administered after 48 hours, but his bowels were not opened till the fifth day, when several large roundworms were passed with the stools. The white-cell count (on the morning after operation) was 12,500, with a normal differential count.

Microscopical examination of the appendix showed marked lymphoid hyperplasia, while that of the lymph node showed reactive hyperplasia with a few eosinophils in the sinuses. The peritoneal fluid contained polymorphonuclear leucocytes, but was sterile.

Case 2

A woman aged 41 gave a history of severe colicky abdominal pain of seven hours' duration. The pain was worst to the right of the umbilicus. She had had nausea from the time of the onset of the pain but had not vomited. Her bowels had not been opened for over 24 hours, and there had been no passage of flatus since the pain had begun. She complained of "feeling obstructed." There were no other symptoms and she could not remember having had a similar attack of pain.

On examination she appeared to have attacks of pain at intervals of about 10 minutes, but her general condition was good; pulse rate was 82 and temperature 98.6° F. (37° C.). There was slight distension of the abdomen, with marked guarding and tenderness to the right of the umbilicus. (Within this area the point of maximal tenderness varied from time to time.) Vigorous bowel sounds were heard on auscultation. Rectal examination was negative and plain films of the abdomen failed to demonstrate any evidence of obstruction. A provisional diagnosis of acute appendicitis was made.

At laparotomy a small amount of fluid was lightly covering the intestine; it was sticky and yellowish in colour. There were over 50 roundworms in the lower ileum, and the small intestine showed alternative areas of segmental spasm. The mesenteric nodes were enlarged, fleshy, and pink. The appendix appeared normal, but was removed. Biopsy specimens were taken of a lymph node and the omentum, and the wound was closed without drainage.

She had a pyrexia of 99° F. (37.2° C.) for three days and then remained apyrexial. She was given 1 oz. (30 g.) of piperazine citrate on the evening of the third post-operative day and passed several roundworms with her stools the next morning. (No antibiotics were used.) The white-cell count (on the morning after operation) was 13,000, with a normal differential count.

Microscopical examination showed an uninflamed appendix with roundworm ova and calcified concretions in the lumen; the lymph node showed reactive hyperplasia, "sinus catarrh"; and the omentum was hyperaemic and congested. The peritoneal fluid contained polymorphonuclear leucocytes and was sterile.

Case 3

A man aged 32 first had "griping" pain in the central abdomen three days previous to being seen. It had continued intermittently and had become progressively worse. He had vomited twice, bringing up bitter yellowish fluid, and had been constipated for three days. He had noticed a loss of appetite over the preceding three months but had had no other symptoms. A history of a similar attack five years ago was obtained; central abdominal pain, vomiting, and constipation had been the symptoms then.

On examination his general condition was good; temperature 98.4° F. (36.9° C.) and pulse rate 88. There was moderate distension of the lower abdomen, with tenderness and guarding to the right of and somewhat below the umbilicus. (The point of maximal tenderness was inconstant, but was confined to the same area.) Rectal examination was negative and a plain radiograph of the abdomen failed to show any evidence of intestinal obstruction. A provisional diagnosis of acute appendicitis was made. At laparotomy the mesenteric glands were enlarged, fleshy, and pink. The intestines were covered with a sticky yellowish fluid and contained about 75 roundworms, the majority in the lower ileum, a few being palpable in the large intestine. There was marked segmental spasm of the small intestine with alternative areas of dilatation. The appendix, a lymph node, and a specimen of the omentum were removed for examination. The wound was closed without drainage.

He had a temperature of about 99° F. (37.2° C.) for six days and then remained afebrile. He was treated for roundworms with 1 oz. (30 g.) of piperazine citrate on the fourth and fifth days, when several roundworms were passed in the stools. On the day after operation the white-cell count was 13,600, with a normal differential count.

Microscopical examination revealed a normal appendix, congestion of the omentum, and marked reactive hyperplasia of the lymph node.

Case 4

A boy aged 15 complained of colicky pain in the central abdomen. The attack had started 36 hours previously, and pain had since increased in severity. It was right-sided, and most severe in the right iliac fossa. He had not vomited, but had complained of nausea. His bowels had not opened for three days, but an enema given shortly before admission had produced some faecal matter containing a large roundworm, about 8 in. (20 cm.) long. The boy had had similar attacks in the past few months and had always been relieved by Ayurvedic remedies for worms except on this occasion.

On examination his general condition was good; his temperature was 99° F. (37.2° C.) and pulse rate 106. The abdomen was not distended, but tenderness and guarding were present to the right of the umbilicus, the point of maximal tenderness being inconstant. Rectal examination was negative. A provisional diagnosis of mesenteric adenitis associated with roundworms was made.

At laparotomy a small amount of clear fluid was found in the peritoneal cavity. The mesenteric nodes of all three groups (juxta-intestinal, intermediate, and terminal) were enlarged, but no worms were palpable in the intestine, which appeared quite normal except for the presence of an uninflamed Meckel's diverticulum. The latter was excised, the appendix was removed, and specimens of the lymph nodes and omentum were taken for biopsy. The wound was closed without drainage.

The patient had a pyrexia of about 100° F. (37.8° C.) for three days. No antibiotics or anthelmintics were given, and he made an uneventful recovery. The white-cell count was 13,200, with a normal differential count, and the stools did not contain any ova or worms. The peritoneal fluid was sterile.

Microscopical examination revealed reactive hyperplasia of the lymph nodes and marked hyperplasia of the lymphoid follicles of the appendix. There was no abnormality of the omentum or the Meckel's diverticulum.

Case 5

A schoolboy aged 16 complained of colicky pain in the right iliac fossa. The pain had started 12 hours previously

and had become worse. He had vomited several times, bringing up small quantities of food and bitter fluid. Bowels had not opened for two days. There were no other symptoms, nor was there a history of having passed worms or having been treated for them.

On examination his general condition was good; temperature 99° F. (37.2° C.) and pulse 115. He was noticeably drowsy. The abdomen was slightly distended, and tenderness and guarding were present in the right iliac fossa. (The point of maximal tenderness was inconstant, but was confined to this area.) Rectal examination was negative. A diagnosis of mesenteric adenitis associated with hyperinfestation with roundworms was made.

Laparotomy disclosed a very small quantity of sticky yellow fluid covering the intestine, and about 75 roundworms in the terminal ileum; there was segmental spasm of the small intestine in the region containing the worms. These findings were associated with well-marked (mesenteric) adenitis affecting all three groups of glands in the mesentery. The appendix appeared normal, but was removed. A lymph node and a piece of omentum were taken for biopsy, and the wound was closed without drainage.

He ran an irregular temperature for five days. Piperazine citrate was given on the fifth night and several roundworms were eliminated next morning. Stool examination on the ninth post-operative day was negative for worms and ova. The white-cell count was 15,800, with a normal differential count, on the day after operation.

Microscopical examination of the appendix showed lymphoid hyperplasia with several ascaris ova in the lumen of the organ; there was marked reactive hyperplasia of the lymph node and congestion of the omentum. The peritoneal fluid was sterile and contained polymorphonuclear leucocytes.

Discussion

Incidence.—Girges (1934), in a comprehensive review of the complications of ascariasis, makes no reference to the association between mesenteric adenitis and hyperinfestation of the small intestine with roundworms. The above five cases occurred in my practice in just over one year, and suggest that the condition must be fairly common, especially when it is remembered that children under 12, in whom complications of roundworms are usually much commoner than in the adult, are not admitted to the General Hospital, Colombo, where this work was carried out.

In the first three cases a provisional diagnosis of appendicitis was made before operation. As the clinical pattern did not quite fit in with that of acute appendicitis a laparotomy through a paramedian incision was performed in each case. In Case 4 a history of the evacuation of a roundworm per anum, combined with a clinical similarity to non-specific mesenteric adenitis, suggested the possibility of this association, but operation did not reveal hyperinfestation, owing, perhaps, to the efficacy of the vermifuge taken. In Case 5 the correct diagnosis was made before operation because the physical sign of drowsiness (in the absence of other signs of toxicity) was added to the clinical features of mesenteric adenitis.

In retrospect it is clear that all five cases presented with the clinical features of acute mesenteric adenitis —namely, generalized abdominal colic, nausea or vomiting, constipation, and pain maximal in an ill-defined area on the right side of the abdomen. There was, however, no history of a recent sore throat or other respiratory infection, as is so often obtained in non-specific mesenteric adenitis. The clinical signs were poorly defined. The temperature was often normal or only slightly raised; the tenderness was usually in the region of the right iliac fosa, but the point of maximal tenderness was inconstant, varying slightly in position with each examination. Guarding rather than rigidity was the predominant feature on palpation of the abdomen, while noticeable distension of the lower abdomen was constantly seen. The cervical lymph nodes were not enlarged, and the white-cell count showed a polymorphonuclear leucocytosis.

The operative findings in each case except the fourth were remarkably constant: a sticky yellow peritoneal fluid lightly covering the intestine, numerous roundworms in the lower ileum, segmental spasm of the intestine, and enlargement of the mesenteric nodes. The fluid was very little in quantity, contained polymorphonuclear leucocytes, and proved to be sterile on bacteriological examination. The roundworms were always large and occupied the "dilated" portions of the bowel. The majority of the worms appeared to be alive, as movement was usually detectable on palpation through the intestinal wall; in some places, however, they were twisted together into bolus-like aggregations. The intestine showed alternate areas of spasm; these segments had the diameter of a lead pencil (about 0.5 cm.), while the dilated portions were only a little larger than normal intestine. The lymph nodes of all three groups — terminal, intermediate, and juxta-intestinal—were involved and they were fleshy, pink, and oedematous. There was never any evidence of suppuration. The parietal peritoneum appeared normal, as did the caecum, appendix, and spleen.

Operative intervention, avoiding undue handling of the intestine, was restricted to removal of the appendix and biopsy of the omentum and a single lymph node. Piperazine citrate was given three to five days after operation, and the patient felt and looked better after the evacuation of worms with the stools. No untoward reaction was observed after the administration of this anthelmintic; in fact, the body temperature reverted to normal in each case after the first post-operative bowel action.

Histological examination showed a normal appendix or lymphoid hyperplasia of the organ. The lymph nodes, on the other hand, always showed reactive hyperplasia — "sinus catarrh." The omentum was hyperaemic and congested.

The chief difficulty in the diagnosis of mesenteric adenitis lies in its resemblance to acute appendicitis. As in some of the above cases, lymphoid hyperplasia may affect both the lymph nodes and the tissue of the appendix, or appendicular colic may be caused by obstruction of the lumen of the organ by ova or worms. It is therefore often difficult to differentiate clinically between mesenteric adenitis and appendicitis. If the diagnosis of the former is suspected, however, the association with roundworms may be surmised from the following features: (1) the absence of a history of a preceding upper respiratory infection; (2) a positive history of the elimination of roundworms by vomiting or per rectum, in the recent past; (3) a history of having begun treatment for worms immediately preceding the onset of symptoms—in this connexion it would appear that piperazine is free of such "toxic" manifestations (Goodwin and Standen, 1958); and, (4) other signs of hyperinfestation, which include drowsiness, irritability, restlessness, or even convulsions (de Silva, 1957).

Operative treatment is desirable, as appendicitis can then be excluded, or it may be found to be superimposed on mesenteric adenitis in association with ascariasis, particularly as worms may initiate inflammation by ulceration of the mucosa, obstruct the lumen of the organ, or cause the appendix to be involved in the lymphoid hyperplasia (see above). Therefore, until some more specific means for detecting *hyperinfestation* is available the wisest course appears to be to perform laparotomy, remove the appendix, and follow this with specific anthelmintic therapy.

While it is possible that mesenteric adenitis is part of an allergic response to hyperinfestation, or is due to infection secondary to mucosal damage by the worms, there is at present insufficient evidence to substantiate these views. The clinical examples, however, show that there is a definite association between the two conditions.

Summary

The surgical complications of infestation with roundworms include intestinal obstruction, perforation, and peritonitis. The available literature makes no mention of an association between ascariasis and mesenteric adenitis. Five cases in which mesenteric adenitis was associated with hyperinfestation with roundworms are described; in only one of these was the correct diagnosis made before operation. The clinical features, the operative and histological findings, and the treatment of this clinical entity are discussed. Until a specific test is available for the detection of hyperinfestation, laparotomy and appendicectomy are recommended, followed by specific anthelmintic therapy.

ADDENDUM.—Since this article was presented for publication two further cases have been encountered: it was possible to diagnose them correctly before operation, and they ran a similar clinical course.

I thank Professor G. H. Cooray for the pathological reports and his help and criticism in the preparation of this paper.

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After the official opening of the Eleventh International Hospital Congress, the inaugural address on the main theme "Efficiency Methods in the Hospital" was given by Dr. T. E. Chester, professor of social administration at Manchester University. He considered that the present interest in efficiency methods was not merely a passing phase, but was becoming a fundamental and essential part of the new equipment of hospitals. The universal steep rise in running costs and the shortages of staff, caused by increased specialization and the change in the social climate in which the hospital has to operate, are but one reason for the need for efficiency methods. Another is the fact that capital expenditure has also risen. . . . The third trend which Dr. Chester distinguished was the increase in the demand for hospital services, coupled with a change in demand. The hospital is no longer a place for poor people in which to die; it has become one of the first essentials of a civilized community. (International Hospital Federation, *News Bulletin*, June, 1959.)

MESENTERIC CYSTS WITH MALROTATED INTESTINE

BY

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Developmental mesenteric cysts are rare. It appears to be more than a coincidence that in four children with this anomaly malrotation of the intestines was also present. The association of these two conditions was first described by Hunter (1922). Subsequent reports have been made by Sala and Nachamie (1929), by Goldberg *et al.* (1940), by Mendillo *et al.* (1952), and by Kron and Satinsky (1954). We have been stimulated to seek for a common factor in their aetiology.

Case 1

A girl aged 6 years was admitted to hospital under the care of Mr. Charles Donald. Intermittent abdominal pain and vomiting started when she was 18 months old, and she vomited once weekly until the age of 4. For the next two years she vomited once a month and the vomitus was always green. Her appetite was poor and her stools had recently become a pale yellow colour.

On examination a smooth, round, mobile cystic swelling 7 cm. in diameter was palpable in the right lower abdomen. The cyst could be freely pushed into the right hypochondrium and into the left iliac fossa.

At laparotomy the cyst was found to be situated "in the wall" of the proximal jejunum, and the blood vessels on its surface were continuous with those encircling the gut. There was a volvulus of the cyst together with the associated jejunal loop, but in addition there was an incomplete rotation of the intestines. The duodeno-jejunal flexure was situated to the right of the midline, and from it a peritoneal band ran laterally across an abnormally high caecum. Division of this band liberated the duodeno-jejunal flexure and the caecum, permitting the display of a mesentery, universal for the small and large gut and having a 5-cm. fenestration at the ileo-caecal junction.

The cyst and the adjacent jejunum were resected, a side-to-side anastomosis restoring intestinal continuity. The mobilized caecum was placed in the left iliac fossa prior to wound closure. Recovery was uneventful and the patient was discharged on the twelfth post-operative day.

Dr. Martin Bodian reported on the excised specimen. "The specimen consists of small bowel 10 cm. in length of normal uniform calibre . . . on its mesenteric border is a spherical cyst 6 cm. in diameter containing almost clear, slightly mucoid yellowish-brown fluid. The smooth, thin fibrous wall of the cyst is covered by serosa and the lining is not loculated. Near the cyst's attachment to the bowel wall the lining is opaque and slightly thickened . . . with raised areas of yellow pigmentation. . . . Microscopy: the cyst wall is formed of collagenous tissue and the lining is a layer of flattened endothelial cells. These appearances are compatible with a diagnosis of mesenteric cyst."

Case 2

A girl aged 4 years presented as an emergency case with a severe attack of abdominal distension and vomiting and

was admitted under the care of Mr. Denis Browne. She had a history of previous similar attacks which were not so severe.

An urgent laparotomy was performed. The abdomen contained over 2 pints (1,140 ml.) of opalescent fluid. There was malrotation of the intestines with a volvulus of the ileum. The gut was mobilized and the volvulus was unwound. Recovery was uneventful and the child was discharged two weeks after operation.

She was subsequently readmitted after an interval of 15 months, having continued to have attacks of abdominal pain and bilious vomiting. A further laparotomy was performed. The lower ileum was found to be obstructed by an omental band and two mesenteric cysts. The compressed ileum was resected together with the cysts, and an end-to-end anastomosis restored the gut. The patient's convalescence was uneventful.

The excised specimen was a loop of ileum patent throughout, with a cyst protruding on each side of the mesentery. One measured 3.5 by 2.5 cm. by 2.5 cm., and the other 6 by 5 by 3 cm. Both cysts contained pale yellow albuminous partly clotted fluid. The cysts were lined with flat endothelium and their thin fibrous walls contained many dilated lymphatic spaces.

Case 3

A girl aged 6 years was admitted to hospital moribund under the care of Professor Moncrieff. She died within half an hour of reaching hospital. This child had a history of intermittent attacks of abdominal pain, vomiting, and constipation since the age of 2½ years. Vomiting was the main feature of the terminal attack, continuing repeatedly for three days prior to admission. Death was due to peripheral circulatory failure.

Necropsy (Dr. Martin Bodian).—The small intestine was found to have undergone a volvulus of two complete turns. The gut was incompletely rotated, with a universal mesentery, high caecum, and abnormal peritoneal bands crossing the duodenal loop. A mesenteric cyst 10 by 6 cm. was related to the lower jejunum. This cyst contained milky fluid, and its congested wall included many dilated lymphatics. Histological examination showed the wall of the cyst to be formed of fibrovascular tissue, lymphatic channels, and thin strands of smooth muscle.

Case 4

A male infant aged 2 days was admitted to hospital under the care of Mr. Charles Donald with a history of bilious vomiting beginning five hours after birth. Intestinal obstruction was diagnosed and exploratory laparotomy revealed chronic meconium peritonitis. The intestines were abnormally rotated in addition to being bound by fibrous adhesions. The transverse colon and mesocolon could not be found. A jejunal stenosis caused obstruction; this was by-passed by a side-to-side anastomosis. The infant survived two days.

Necropsy (Dr. Martin Bodian).—A little faecal matter oozed from the anastomosis, and the jejunum was friable, congested, and distended. The intestinal loops adhered and the mesenteric lymph nodes were haemorrhagic. 33 cm. proximal to the ileo-caecal valve there was an abrupt and extreme stenosis, and distal to this point there was a fenestrated mesentery and a mesenteric cyst which contained a little yellowish-brown fluid. This cyst was gangrenous and unsuited to histological examination, but the adjacent tissue showed the appearances of chronic meconium peritonitis. The unexpanded transverse colon was found behind the stomach and there was no gastro-colic ligament.

Discussion

The incidence of mesenteric cysts has been estimated by Beahrs and Judd (1947) as seven cases in a million hospital admissions. When some of these rare lesions are associated with malrotation of the gut the possibility of a common factor in the aetiology of the two conditions is suggested. A close study of the relevant literature revealed two complementary hypotheses to link these lesions, and to these we now add a third.

The standard description of the rotation of the gut is that of Frazer and Robbins (1915), the embryology of the anomalies being discussed by Dott (1923). It is at the tenth week of foetal life, during the second stage of rotation (which comprises the return of the mid-gut loop to the abdominal cavity), that most anomalies occur. Dott considers that these are due to variation of the size of the embryonic umbilical orifice, which is normally too narrow to permit the bulky hernial content to return *en masse*. Hunter (1922) suggested that if the hernial bulk was enlarged by a mesenteric cyst normal return and rotation would be impeded.

This hypothesis requires the cyst to be of a significant size by the tenth week of foetal life, and this possibility is confirmed by the work of Lewis and Thyng (1908). They observed a cyst in the duodenal mesentery of a 20-mm. embryo pig, equal in diameter to the lumen of the gut. It appeared to arise by sequestration from an intestinal diverticulum, and their extensive study of the comparative embryology in the pig, rabbit, and man led them to conclude that similar diverticula were constantly present in the human embryo, commonly from the distal ileum, where many cysts are known to occur.

Mesenteric cysts can also develop in other ways. Their range, variety, and classification, have been the subject of many reviews such as those of Moynihan (1897) and Higgins and Lloyd (1924). The latter authors emphasize that true mesenteric cysts are not malignant, dermoid, or parasitic and do not arise in any normally placed retroperitoneal organ. These cysts have been found in the foetus and at every age to the eighth decade. Their diameter can vary from a few millimeters to a size that all but fills the abdomen, and their contents, irrespective of their nature, may include chyle or blood (Dowd, 1900). Mesodermal remnants, derived from the Wolffian body or from lymphatic or vascular tissue, account for most of these lesions that are not of intestinal origin. The latter group are to be clearly differentiated from duplications of the intestine both in structure and in aetiology, but as duplications arise in comparable situations in the sixth week of foetal life (Bremer, 1944) their mechanical effects on gut rotation may be similar.

A distinct group of mesenteric cysts of intestinal derivation is that associated with anterior spina bifida. Saunders (1943) reviewed this subject and observed that the cysts and adjacent bowel are tethered to the defective vertebral bodies by strands of connective tissue. This embryonic dorsal tethering of the gut (which can exist with an occult vertebral lesion and without cyst formation) can lead to malrotation. The vertebrae in our cases were not examined with this possibility in view. The fundamental anatomical lesion in the teratology of this anomaly is probably a sagittal split in the notochord with contact of the dorsal ectoderm with the yolk sac endoderm.

Foetal necrosis overtakes most of the relatively common small cystic formations in the mesentery of the embryo. We now suggest that occasionally this atrophy may cease and the cyst enlarge because of the recurrent disorganization of its lymphatic and venous drainage as a result of repeated volvulus of the mid-gut

loop. This form of volvulus is recognized as a frequent complication of intestinal malrotation.

Summary and Conclusions

The cases of four children are described in which that rare condition developmental mesenteric cyst was associated with malrotation of the intestines.

Mesenteric cysts often present clinically with intestinal obstruction resulting from volvulus. Whilst the volvulus is often confined to the intestines immediately adjacent to the cyst, it occasionally involves the mid-gut loop, and it is then associated with incomplete or aberrant rotation of the intestines. It is therefore prudent to examine the rotation of the gut when operating for mesenteric cysts. Conversely, the presence of mesenteric cysts should be excluded in patients with malrotated intestines, even when volvulus of the mid-gut loop is not apparent at laparotomy.

We thank Mr. Denis Brown, Professor Alan Moncrieff, Dr. Martin Bodian, and the late Mr. Charles Donald, of the Hospital for Sick Children, Great Ormond Street, London, for permission to report the cases, and Mr. H. H. Nixon and Mr. W. M. Dennison for their help and advice.

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Medical Memoranda

Two Cases of Pubopenile Testis

Ectopic testes may be found in various positions. Wakeley (1953), who reviewed the embryology of this condition, stated that among the least common positions are the perineal, the pubopenile, the femoral or crural, and the transverse.

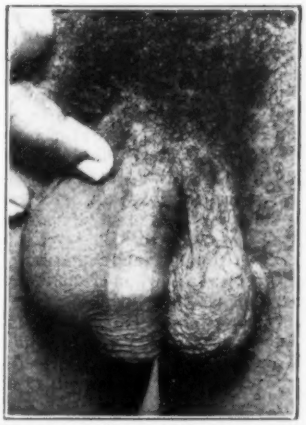
In the Nosological Index of St. Thomas's Hospital, dating back to 1937, there are only three cases of uncommon ectopic testes, one being perineal and two, reported below, being pubopenile.

This pubopenile type is rare, only seven cases being recorded in the literature. Popow (1888) and Poupart (1897) reported the first two from France, followed by Bernhard (1925) and Kausch (1925), who each reported a case from Germany. Moynihan (1924) and Forsyth (1924) reported the only ones in this country from Leeds, and Kaufman (1943) recorded the first and only one from the U.S.A.

In most cases the patient is brought to the doctor when young because the parents notice one or both testes to be absent. With the influx of British West Indians into this country, numerous congenital abnormalities are being first noted in adults, as their parents do not bother to seek advice so readily.

Case 1.—A sixteen-year-old London boy was referred by his doctor to the genito-urinary department complaining of having had pain in his right groin for three months. On examination he was found to have normal secondary sexual characteristics for his age, but had a left ectopic testicle lying at the root of his penis. He was later admitted to hospital, and at operation the testicle was dissected free from the pubis and successfully transferred into the scrotum.

Case 2.—A misplaced testis was found on routine examination of a 25-year-old Jamaican, who reported for treatment of acute gonorrhoea in the department of venereal diseases. His right testicle, which was fully developed, was found to be lying subcutaneously on the dorsal surface of his penis (see photograph). It could be easily pushed back up to the root of the penis, but not round to the sides. He stated that it caused him no inconvenience in its present position, as it retracted easily to the root of his penis, where it had lain in his younger days. He was referred to the genito-urinary department for opinion and advice, and, although advised to have an orchiopexy, he failed to report for operation.



Photograph of the misplaced testis of Case 2.

I thank Mr. T. W. Mimpriss and Dr. C. S. Nicol for permission to report these cases, and for their encouragement and advice. I am also indebted to the photographic department of St. Thomas's Hospital for the photograph.

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Riedel's Thyroiditis

In 1896 and 1897 Riedel described three cases of a peculiarly hard infiltrating lesion of the thyroid which was thought to be malignant both clinically and at operation, but histological examination and subsequent clinical course showed the disease to be a chronic inflammatory process. The condition is rare enough to warrant placing on record a case which conforms to the original description given by Riedel.

CASE REPORT

The patient was a woman aged 52. In 1951 she complained of a lump in the left side of her neck. There were no other subjective symptoms. Examination revealed a

stony-hard mass apparently occupying the left lobe of the thyroid and firmly adherent to surrounding structures, but not to the skin. The B.M.R. was +7%; Hb, 82%; cholesterol, 186 mg. per 100 ml. A provisional diagnosis of carcinoma was made.

Operation (Miss G. M. Barry).—The mass was found to involve the whole left lobe of the thyroid, and no normal tissue was evident. It was bound to all the surrounding structures, including the muscles and jugular vein. The right lobe of the thyroid appeared normal. Owing to the dense adhesions resection was abandoned, but a biopsy specimen was obtained.

Biopsy (Fig. 1).—The report stated: "The specimen consists largely of dense granulation and fibrous tissue with considerable hyalin collagen. Some surviving thyroid follicles can be seen to the upper end of the section, with fibrous tissue penetrating between them. The capsule of the thyroid has been broken through by this inflammatory tissue and in places infiltrates voluntary muscle. Some small blood vessels show obliterative endarteritis."

The patient made an excellent post-operative recovery and declined further treatment.

She was next seen in 1956, when she complained principally of tiredness and lethargy. The lump in her neck was still present and, though she thought it had not changed, the isthmus was now involved. She was clinically anaemic.

Investigations.—Hb, 7.5 g. (51%); R.B.C., 2,950,000; P.C.V., 25%, M.C.V., 92.5 cubic microns; M.C.H.C., 31%, W.B.C., 7,000 (neutrophils 71%, lymphocytes, 16%, monocytes, 10%, eosinophils, 3%). Marrow obtained with

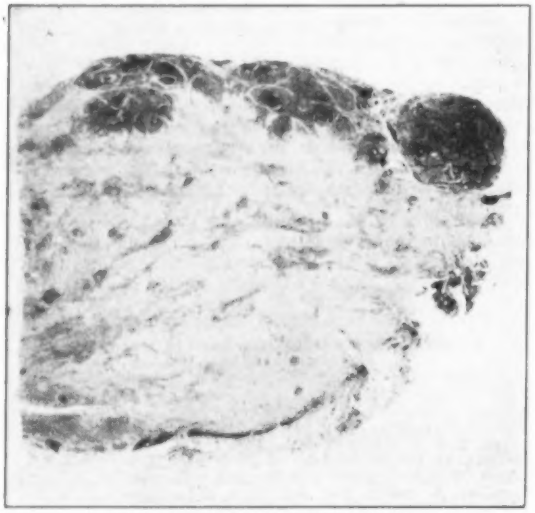

FIG. 1.—Biopsy specimen (×4.4.)

difficulty. General hypoplasia with specialized depression of erythropoietic activity. No abnormal cells. Normal hydrochloric acid in gastric contents. E.S.R. 30 mm. in one hour (Westergren). Precipitation test (Dr. D. Doniach) was negative, but further tests with complement fixation and tanned red cells showed the presence of a weakly positive antibody. Thymol turbidity, 14 units; colloidal gold, 2; zinc sulphate, 14. ^{131}I test showed normal thyroid function. Cholesterol 190 mg. per 100 ml. A neck scan (Fig. 2) showed that activity was confined to the right lobe.

The patient was put on 30 mg. cortisone daily; her haemoglobin rose to 80%, and was accompanied by a return to her normal strength and energy. No change has yet been apparent in the thyroid gland.

COMMENT

Cases of true Riedel thyroiditis are very rare, but probably do represent a specific entity, the cause of which is not yet determined (Graham, 1931). Woolner *et al.* (1957) report an incidence of 0.05% in 42,000 thyroid operations, and Harland and Frantz (1956) report only eight in 34 years of thyroid surgery.

The majority of patients complain only of a lump in the neck. Clinically this is of a peculiar hardness, justifying the term used by Riedel of "Eisenharte strumitis." The diagnosis of carcinoma cannot be excluded even at

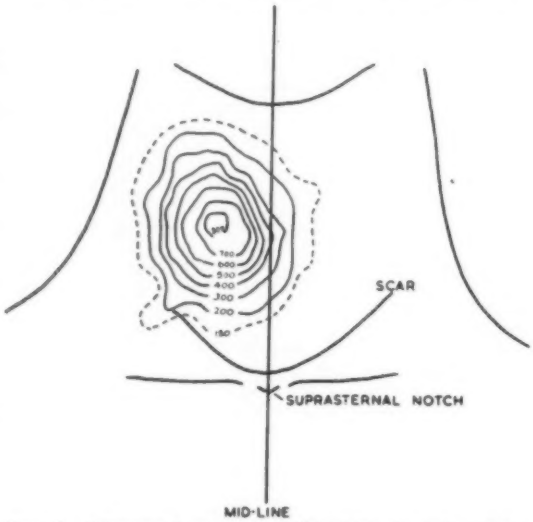

FIG. 2.—"Contour" map of radioactivity in neck. Ekco scintillation counter. Counts per 5 seconds. Background, 70 counts per 5 seconds.

operation, and the lesion is probably basically ineradicable. The diagnosis can be made only on histological grounds, and this demands evidence of replacement of thyroid tissue by dense solid fibrous tissue, extending beyond the confines of the thyroid gland and invading the surrounding tissues. The subsequent clinical course confirms the simple nature of the lesion, and also shows that there is nothing to be gained by attempting to remove the lesion completely by surgical means (Woolner *et al.*, 1957).

All patients in whom the disease is unilateral remain euthyroid, as does our patient after an interval of five years. However, she gives evidence that there is still some systemic disorder. She still shows protein abnormalities, with raised E.S.R., altered turbidity tests, and the presence of a weakly positive antibody. The anaemia is as yet unexplained, and may also be evidence of a long-continued systemic disorder. Its response to cortisone is probably not specific.

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Reviews

HAEMATOLOGY UP TO DATE

British Medical Bulletin. Volume 15, No. 1. *Haematology.* (Pp. 88; illustrated. 20s.) London: Medical Department, British Council. 1959.

Haematology has expanded rapidly in the past few years, and there is a need for periodic up-to-date reviews of this subject so that those interested can assimilate what is new. Such a review is provided in this number of the *British Medical Bulletin* by 14 contributors, all of whom are acknowledged experts in their particular fields.

The subject matter includes descriptions of our present knowledge of iron metabolism, the normal and abnormal absorption of vitamin B_{12} as studied by the use of the radioactive-cobalt-labelled substance, and the role of folic acid in the treatment of various blood disorders. Haemoglobin synthesis, the chemistry of abnormal haemoglobins and their inheritance, and the relationship of foetal haemoglobin to disease are all discussed in full. A section on cytology includes descriptions of methods for studying the pathway of cellular development by bone-marrow culture, and a new concept of the life-cycle of the lymphocyte which suggests that all the original opinions of life span and fate of the lymphocyte have been wrong. Descriptions of the methods for studying red-cell survival and diagnosing the presence of immune bodies in acquired haemolytic anaemia bring the reader up to date with this very important subject. Investigation of the structure and metabolism of the red cells in certain haemolytic syndromes has opened up what to many must be an entirely new field. The problems of leukaemia are dealt with by studies of the epidemiology and treatment.

Faults are few, and the only criticism that can be levelled is that some authors have failed to guide the reader adequately in the practical application of this new information to the everyday clinical problem. For example, a more specific description of the changes that these advances have made in the diagnostic criteria of thalassaemia would have been welcome. But this does not detract from the value of this *Bulletin*, which should be read by all who have an interest in the study of the blood, be he clinician, pathologist, biochemist, or student.

A. A. SHARP.

EXPERIMENTAL MYOCARDIAL NECROSIS

The Chemical Prevention of Cardiac Necroses. By Hans Selye, M.D., Ph.D., D.Sc. (Pp. 235+ix; illustrated. $7.50.) New York: The Ronald Press Company. 1958.

This monograph can be recommended to those with a particular interest in myocardial function. It contains an account of the experimental production of myocardial necrosis in animals, chiefly in the rat, after the administration of various hormones, electrolytes, and vitamins. Dr. Selye approaches his subject with the general hypothesis that hormones can, without themselves producing disease, so condition the body's response to normally inoffensive agents that morbid changes result. He then proceeds to describe the injurious and the protective effects of many electrolytes and steroids on the myocardium. For example, in rats suitably conditioned with corticoids the administration of certain sodium salts resulted in myocardial necrosis, while potassium and magnesium salts and certain chlorides prevented this development. Similarly, when "sub-threshold" doses of steroids were given to rats a variety of non-specific noxious agents such as heat, cold, trauma, and exertion consistently resulted in myocardial necrosis, which could be prevented by the simultaneous administration of certain electrolytes.

Some may feel that too little attention has been given both to the role of ischaemia in the production of myocardial infarction and to the more orthodox explanations of the sequence of events leading to myocardial necrosis. Others may not agree that infarcts which occur without associated coronary occlusion in humans can be regarded as clinical counterparts of the toxic necrotizing myocarditis produced by various agents in animals. Nevertheless, this attempt to explore some of the relationships between the actions of steroids and the actions of electrolytes is stimulating. Far too little attention has been given to metabolic factors which may determine whether the myocardium will withstand or succumb to circulatory inadequacy, and Dr. Selye's experimental approach will be followed closely.

M. F. OLIVER.

TWENTY THOUSAND NURSES

Twenty Thousand Nurses Tell Their Story. By Everett C. Hughes, Helen MacGill Hughes, and Irwin Deutscher. (Pp. 280+xi. 45s.) Philadelphia and Montreal: J. B. Lippincott Company. London: Pitman Medical Publishing Co. Ltd. 1958.

This book gives a revealing picture of nurses and the transitional stage which nursing has reached to-day in America. Written by three sociologists, it is a readable volume of some 300 pages based on studies of nursing functions initiated in 1951 by the American Nurses' Association. The findings deserve close attention, being pertinent to a great extent also in this country.

The studies analyse the social background of nurses, their opinions of themselves and their work, and other people's opinions; relationships with patients, doctors, and colleagues; opportunities for marriage, family life, and citizenship as well as a career in nursing. Others deal with training and recruitment; with nursing service in hospitals, large and small, and in special branches, particularly industry, and with private nursing and psychiatric nursing.

The most pressing problem, which received detailed attention, was the division of nursing tasks between registered and practical nurses and nurse aides. Some senior nurses described the present situation as chaotic. The work has expanded, the number and kinds of personnnel have increased, and no one has yet settled the best division. The doctor undertakes many techniques at first, but as he becomes too busy the ubiquitous and competent nurse takes over. "If the registered nurse has left the bedside it is because the doctor has filled her time for her in other ways." "Touch tasks" are now largely in the hands of auxiliaries; the nurse aide is likely to provide more direct patient care than even the practical nurse. The questions, Who does it? Who is supposed to do it?, are answered differently from hospital to hospital and on different shifts in the same hospital. In one survey professional nurses were found to be doing 31% of sterile and 40% of unsterile treatments, while the

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non-professional ranks were doing 44% of the sterile and 22% of the unsterile treatments.

One of the monographs classified nurses as: the professionalizers (those who stand for knowledge and look on healing as the rational application of medical science); the traditionalizers (the dedicated type); the utilizers (to whom nursing is just a job). A group, which may also be found in any institution, is also described as the "home-guard"—the old faithfuls who stay on in the comfortable berth they have built up, giving the institution its special character, setting its tone, and becoming immensely powerful—for good or ill.

Nurses claimed that patient care was the outstandingly satisfying part of their work, but graduate nurses are increasingly occupied with supervisory and administrative duties without being given authority equivalent to that of doctors or administrators. The frontier of duty between the registered nurse and the doctor is very vulnerable to abuse. As nurses take over more of the procedures formerly done by doctors they may find themselves actually breaking the law. The legal position of the nurse varies in the 49 States, but it seems generally true that the nurses' work is outgrowing the legal definition of it.

The authors suggest that the time has come for something more than a reallocation of tasks and that psychiatry is to be thanked for reminding the medical profession, split as it is into specialties usually named for parts of the body, of the supreme importance of "the whole person." If bedside tasks are to become the kingdom of the auxiliary, the professional nurses might turn to the cultivation of skills in human understanding and appreciation, with new emphasis on social psychology in their training. That such skills are lacking is shown by the comments of patients, particularly in a large maternity centre. "Not more care of the patient but a different kind of care is the crux of the matter."

MARJORIE L. WENGER.

TRANQUILLIZERS IN SKIN DISORDERS

Psychotherapeutic Drugs. By Ashton L. Welsh, M.S., M.D. (Pp. 139+xiii. 36s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1958.

This book has a deceptive title, for it is written by an American assistant professor of dermatology and syphilology rather than by a psychiatrist or general physician. It lists all the various tranquillizers now in use, with their complications, particularly dermatological ones, and also reports some dermatological findings in the use of these various tranquillizing agents in skin conditions. The author reports that by the time skin patients were sent to him for consultation half of them were already on tranquillizers. This suggests that much greater importance is placed on the emotional causes of skin disorders in America than in this country.

Those who buy this book because they think they will get help from it in the use of drugs for psychotherapeutic purposes, as the title suggests, are going to be gravely disappointed. All that they will get are a few psychological platitudes and a sketchy summary of some of the psychiatric literature on the various drugs. A much better title would have been "The Use of Tranquillizers in Skin Disorders," for this is what the book is really about, but probably under this title it would not have sold half so well.

WILLIAM SARGANT.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

A Defence of Free Learning. By Lord Beveridge. (Pp. 146+xiv. 18s.) London: Oxford University Press. 1959.

Les Formes Viscérales des Phacomatoses. By Dr. Jean Schmitt. (Pp. 279; illustrated. 2,800 fr.) Paris: G. Doin et Cie. 1959.

Les Dysraphies de l'Axe Nerveux et de ses Enveloppes Cranio-Rachidiennes. Étude Critique du Status Dysraphicus. By Dr. P. Tridon. (Pp. 235; illustrated. 2,300 fr.) Paris: G. Doin et Cie. 1959.

The Principles of Humane Experimental Technique. By W. M. S. Russell, M.A.(Oxon.), D.Phil.(Oxon.), and R. L. Burch. (Pp. 238+xiv; illustrated. 30s.) London: Methuen and Co. Ltd. 1959.

Annual Review of Medicine. Vol. 10. Edited by David A. Rytand and William P. Creger. (Pp. 448+vii. $7.50.) Palo Alto, California: Annual Reviews, Inc. 1959.

Chirurgie der Wirbelsäule und des Rückenmarks. By Dr. Felix Jaeger. With a contribution, ***Die Chirurgie der Wirbeltuberkulose.*** By Dr. Josef Kastert. (Pp. 190+viii; illustrated. DM. 59.) Stuttgart: Georg Thieme Verlag. 1959.

The Church's Ministry of Healing. By A. H. Purcell Fox, A.K.C. (Pp. 115+xiv. 10s. 6d.) London: Longmans. 1959.

Family and Class Dynamics in Mental Illness. By Jerome K. Myers and Bertram H. Roberts. (Pp. 295+xi. 56s.) New York: John Wiley and Sons, Inc. London: Chapman and Hall, Limited. 1959.

Parsons' Diseases of the Eye. Thirteenth edition. By Sir Stewart Duke-Elder, G.C.V.O., Ph.D., D.Sc., LL.D., M.D., F.R.C.S., F.R.A.C.S., F.A.C.S. (Pp. 613+viii; illustrated. 50s.) London: J. and A. Churchill Ltd. 1959.

Red Cross International and the Strategy of Peace. By James Avery Joyce. (Pp. 270+xii; illustrated. 25s.) London: Hodder and Stoughton. 1959.

Psychiatrische und Nervenklinik. Krankenvorstellungen. By Kurt Kolle. (Pp. 252+xvi. DM. 19.80.) Stuttgart: Georg Thieme Verlag. 1959.

ABC für Zuckerkranke. Ein Ratgeber für den Kranken. Tenth edition. By Prof. Dr. Ferdinand Bertram. (Pp. 88. DM. 4.20.) Stuttgart: Georg Thieme Verlag. 1959.

Symposium über Aktuelle Fragen der Anästhesiologie. Edited by Dr. Lothar Barth. (Abhandlungen der Deutschen Akademie der Wissenschaften, Klasse für Medizin, Jahrg. 1958, Nr. 1.) (Pp. 115; illustrated. DM. 13.50.) Berlin: Akademie Verlag. 1959.

World Directory of Venereal Disease Treatment Centres at Ports. (Pp. 162. 8s. 6d.) Geneva: World Health Organization. 1959.

The Life and Times of Sir Charles Hastings. By William H. McMenemey, M.A., D.M., F.R.C.P.I., D.P.M. (Pp. 516+xii; illustrated. 50s.) Edinburgh, London: E. and S. Livingstone Ltd. 1959.

General Register Office. Studies on Medical and Population Subjects: No. 15. Social and Biological Factors in Infant Mortality. By J. A. Heady, M.A., and M. A. Heasman, M.R.C.S., L.R.C.P., D.P.H. (Pp. 195+viii. 20s.) London: H.M. Stationery Office. 1959.

The Clonal Selection Theory of Acquired Immunity. By Sir Macfarlane Burnet, O.M., F.R.S. (Pp. 209+ix. 22s. 6d.) London: Cambridge University Press. 1959.

Radiographic Atlas of Skeletal Development of the Hand and Wrist. Second edition. By William Walter Greulich and S. Idell Pyle. (Pp. 256+xvi; illustrated. £6.) Stanford, Cal.: Stanford University Press. London: Oxford University Press. 1959.

The Postnatal Development of the Human Cerebral Cortex. By J. LeRoy Conel. Vol. VI. The Cortex of the Twenty-four-month Infant. (Pp. 310; illustrated. £5.) Cambridge, Massachusetts: Harvard University Press. London: Oxford University Press. 1959.

The Collected Statistics of Malignant Disease seen at University College Hospital, London, during the Period 1946-1950. Compiled by the Cancer Follow-up Department, University College Hospital, London. (Pp. 632+vii. £5.) Shrewsbury: Wilding and Son Limited. 1958.

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COR PULMONALE AND CARDIAC FAILURE

Cor pulmonale, or pulmonary heart disease, exists when the heart reacts abnormally to pulmonary insufficiency. It may be acute or chronic, and the pattern of response depends upon the degree of pulmonary vascular resistance and the severity of respiratory failure. In the earlier stages hyperventilation and increased cardiac output compensate for the pulmonary deficiency, giving the classical features of the hyperkinetic circulatory state, with central cyanosis, warm extremities, and a full arterial pulse. Later the heart may fail through hypoxia or an inability to overcome pulmonary hypertension, and then peripheral cyanosis, coolness of extremities, and a low amplitude pulse are likely to develop.

Chronic bronchitis and emphysema probably account for not less than nine-tenths of all cases of cor pulmonale, but the progressive pulmonary insufficiency in its advanced stages by no means necessarily embarrasses the heart. Indeed, a healthy heart is a remarkably vigorous organ, and increasing hypoxia and hypercapnoea may easily incapacitate some other part, such as the respiratory centre, long before the heart shows signs of strain. Hence studies of the frequency of cor pulmonale associated with cardiac failure do not necessarily reflect the prevalence of chronic bronchitis and emphysema, and valid comparisons with, for example, air pollution or living conditions may not be easy. An additional pitfall in such studies is the difficulty in diagnosing cor pulmonale. A history of recurrent bronchitis with increasing dyspnoea and the characteristic physical signs enable the pulmonary aspect to be assessed with reasonable certainty; but the age group most closely concerned—men over 50—is likely to carry an appreciable load of ischaemic heart disease and hypertension, so that the apportionment of damage between the heart and lungs may be difficult at times, particularly in those who die within a few hours of coming under medical observation. Admittedly radiological and electrocardiographic studies may help, but they are not infallible.

From time to time efforts have been made to determine the relative frequency of cor pulmonale as a cause of cardiac failure. P. Wood[1] estimated that it accounted for between 5 and 10% of all forms of heart disease, which is similar to the American experience of R. W. Scott and C. F. Garvin,[2] who attributed 6.3% of 790 cardiac deaths to cor pulmonale secondary to emphysema. On the other hand, F. J. Flint[3] thought that cor pulmonale existed in one-quarter of all patients admitted with cardiac failure to the City General Hospital, Sheffield. In order to explore further this discrepancy, Professor C. H. Stuart-Harris and his colleagues undertook a survey of all patients admitted to various hospitals in the Sheffield hospital region suffering from cardiac failure during the period 1954 to 1956. Their report is published in the opening pages of this issue of the *Journal*. The ages of the 487 patients studied were from 15 to 69. Of these cases 172 (35%) were classified as cor pulmonale, 165 (34%) as ischaemic and/or hypertensive heart disease, 106 (22%) as rheumatic carditis, and the remaining 44 (9%) came into a miscellaneous category. The figure for cor pulmonale is striking and is even higher than Flint's estimate; it was 41% in Sheffield alone and 30% in the other hospitals in less highly industrial parts of the region. Males preponderated in the ratio of 3.5 to 1.

Chronic bronchitis and emphysema are known to be exceedingly common in the industrial areas of the north of England, so that the incidence of cor pulmonale might also be expected to be high. Whether the prevalences of these pulmonary and cardiac conditions necessarily go hand in hand is a matter for conjecture. Certainly they both seem to be influenced by the same external factors. Stuart-Harris's figures, which he admits are rather small, strongly suggest that residence in an industrial environment and heavy cigarette smoking predispose to cor pulmonale. The seriousness of cor pulmonale with cardiac failure is well known, and few patients survive the first attack of cardiac failure for more than two years: of Stuart-Harris's 172 patients, 38% died in hospital.

[1] Wood, P., *Diseases of the Heart and Circulation*, 1956, London.
[2] Scott, R. W., and Garvin, C. F., *Amer. Heart J.*, 1941, **22**, 56.
[3] Flint, F. J., *Lancet*, 1954, **2**, 51.

THE GLOMERULUS IN THE NEPHROTIC SYNDROME

The nephrotic syndrome consists of albuminuria, hypoalbuminaemia, generalized oedema, changes in the levels of the plasma globulins, and hypercholesterolaemia. Of these, the essential features are albuminuria and hypoalbuminaemia. The syndrome may result from several different renal

diseases. These are glomerulonephritis, particularly the membranous or Ellis type II variety; diabetic glomerulosclerosis; amyloid disease; thrombosis of the renal vein; disseminated lupus erythematosus; chronic heavy-metal poisoning, especially by mercury; and possibly genetically determined disease of the nephron and renal arteriolosclerosis. There may be others.

Generalized oedema results from the lowered concentration of albumin in the plasma. This change lowers the colloid osmotic pressure of the blood and leads to a reduction of plasma volume. Reabsorption of sodium by the renal tubules is increased, and the secretion of aldosterone may be. Consequently the tissues of the body retain electrolytes and water. It is now clear that the cause of the hypoalbuminaemia is the continued loss of albumin from the plasma into the urine. Thus it has been established that urinary albumin has the same characteristics as plasma albumin on electrophoresis[1] and that the two proteins are identical immunologically.[2–4] The incorporation of heavy nitrogen into the two proteins follows the same course, and this experiment shows that the urinary albumin is in fact a sample of the plasma albumin circulating at the time.[5]

Many investigators have thought that the liver should be able to synthesize enough albumin to make good the urinary losses and to maintain the plasma level at a normal value. It has been suggested, therefore, that patients with the nephrotic syndrome may have some metabolic defect which leads either to inadequate synthesis or to increased katabolism of plasma albumin. However, in the nephrotic syndrome there is no evidence of any disturbance of protein metabolism which is not a consequence of proteinuria. A decline in the plasma levels of individual protein fractions almost always bears a relationship to their urinary clearances. Increased plasma levels of certain globulins and of cholesterol are less easy to explain, but these phenomena, too, appear to be a result of albuminuria.

Until recently the pathology of the nephrotic syndrome was interpreted from the post-mortem findings. Now these are being supplemented by data from percutaneous renal biopsy. This technique is limited by the small amount of tissue which can be examined, but it has the merit that progress can be studied by repeated biopsy. These studies have confirmed the importance of membranous or type II glomerulonephritis and of amyloid disease and also revealed that in some cases the kidney was apparently normal.[6,7] The changes characteristic of type I glomerulonephritis, of disseminated lupus erythematosus, diffuse diabetic glomerulosclerosis, and renal vein thrombosis have also been found.[8] Recently A. M. Joekes and his colleagues have added the name of focal glomerulonephritis to this list, using the word in a purely descriptive, histological sense.[9] The lesions in this group have some of the features of both type II nephritis and of disseminated lupus erythematosus, and cases of this type have in fact been classified by other workers as early type II nephritis.[10] Whether "focal glomerulonephritis" as described by these authors is in fact a different disease from type II glomerulonephritis needs further study. In any case it is distinct from the "focal embolic nephritis" of subacute bacterial endocarditis and the "focal nephritis" associated with recurrent streptococcal infection. Joekes and his colleagues also report three cases of nephrotic syndrome in which the kidney showed benign nephrosclerosis. Two of these patients had received organic mercurials as diuretics but one had not.

The glomerular changes characteristic of membranous or type II nephritis[11,12] are thickening of the basement membrane, accentuated lobulation of the tufts, increased cellularity, and hyalinization, but some of these changes may be found in almost all diseases causing the nephrotic syndrome, even renal vein thrombosis.[9] For this and other reasons there is some doubt about the specificity and significance of such changes in the kidney in cases of the nephrotic syndrome.

The study of this difficult problem has been carried a stage further by recent important work on the electron microscopy of ultra-thin sections of the kidney. Thus the significance of thickening of the glomerular basement membrane as revealed by light microscopy has been rendered more doubtful by the observation that under electron microscopy this structure consists of at least three components—the basement membrane proper, attenuated processes of endothelial cytoplasm, and the foot processes of

[1] Luetscher, J. A., Jr., *J. clin. Invest.*, 1940, **19**, 313.
[2] Squire, J. R., in *Advances in Internal Medicine*, 1955, edited by W. Dock, and I. Snaffer, Chicago, **7**, 201.
[3] Gitlin, D., *Amer. J. Dis. Child.*, 1952, **83**, 82.
[4] Gell, P. G. H., *Biochem. J.*, 1955, **59**, viii.
[5] Spector, W. G., *Clin. Sci.*, 1954, **13**, 1.
[6] Bjorneboe, M., Brun, C., Gormsen, H., Iversen, P., and Raaschon, F., *Acta med. scand.*, 1952, suppl. 266, 233.
[7] —— —— —— —— ——, ibid., 1952, suppl. 266, 249.
[8] Pollak, V. E., Kark, R. M., Pirani, C. L., Soothill, J. F., and Muehrcke, R. C., *J. chron. Dis.*, 1957, **5**, 67.
[9] Joekes, A. M., Keptinstall, R. H., and Porter, K. A., *Quart. J. Med.*, 1958, **27**, 495.
[10] Ross, J. H., and Ross, I. P., *Lancet*, 1957, **2**, 559.
[11] Ellis, A., ibid., 1942, **1**, 34.
[12] —— ibid., 1942, **1**, 72.
[13] Hall, B. V., *Proceedings of 6th Conference on the Nephrotic Syndrome*, 1954, National Nephrosis Foundation, Inc., New York.
[14] Farquhar, M. G., Vernier, R. L., and Good, R. A., *Amer. J. Path.*, 1957, **33**, 791.
[15] Meriel, P., Sorel, R., Suc, J. M., Putois, J., Regnier, C., and Dupont, H., *Sem. Hôp. Paris*, 1958, **34**, 1673.
[16] Oliver, J., *J. Mt Sinai Hosp.*, 1948–9, **15**, 175.
[17] Rather, L. J., *Medicine (Baltimore)*, 1952, **31**, 357.
[18] Gregoire, F., Malmendier, C., and Lambert, P. P., *Amer. J. Med.*, 1958, **25**, 516.

epithelium.[13] Electron microscopy of specimens obtained by renal biopsy from cases of the nephrotic syndrome indicates that the essential lesion is loss of the normal epithelial foot processes, with an increase in intracytoplasmic droplets in these cells.[14 15] As the disease progresses the basement membrane becomes thickened, its endothelial border blurred and irregular, and the structure loose in texture and no longer homogeneous. The luminal border of the endothelium then becomes irregular and the cyotplasmic droplets increase in number.[14] It may be that the epithelial foot processes are essential for the normal semi-permeability of the glomerulus, and their disappearance may herald the onset of heavy albuminuria and represent the basic lesion of most cases of the nephrotic syndrome.[13 14]

The precise role of the renal tubules in the nephrotic syndrome remains in doubt. Whatever the underlying lesion, the cells of the proximal tubules usually show hyaline and fatty droplets in their cytoplasm. Hyaline droplets consist chiefly of reabsorbed protein,[16] and the intracytoplasmic lipoid probably represents both reabsorbed lipoprotein and also possibly a manifestation of disturbed cellular metabolism as in the liver. Sometimes the tubules show dilatation of the lumen and flattening of the lining epithelium. There seems to be no particular correlation between the presence of such tubular "atrophy" and the nature of the glomerular lesion. Even in cases thought to be due to chronic mercurial intoxication the tubular changes may be no more dramatic.[9]

The glomerular filtrate normally contains protein, though it is reabsorbed by the tubules before reaching the ureter.[17] This means that proteinuria in the nephrotic syndrome could be due both to increased permeability of the glomerulus and to diminished reabsorption. If valid inferences can be made from data obtained from animal experiments, it appears that the major cause of proteinuria in the nephrotic syndrome due to amyloid disease and glomerulo-nephritis of types I and II is increased glomerular permeability, but that some diminished tubular reabsorption probably occurs as a secondary phenomenon.[18] This finding is in accord with the evidence provided by light and electron microscopy. Evidence of tubular dysfunction such as glycosuria or aminoaciduria occasionally occurs, especially in children, but this too may be a secondary phenomenon.

The high-protein diets given in treatment, even if unable to influence the level of plasma albumin, help to combat the malnutrition from which these patients often suffer. Restricting the intake of sodium helps to reduce oedema, and this can also be achieved effectively with the aid of cationic-exchange resins. The diuretic chlorothiazide, which is safer than the organic mercurials, may prove a valuable therapeutic measure. The intravenous infusion of concentrated salt-free serum albumin sometimes leads to diuresis and the disappearance of albuminuria, with the resultant remission of oedema and hypoalbuminaemia. It is probable that such results can be achieved only in cases with little structural damage to the glomerulus. Early or mild examples of type II glomerulonephritis may fall into this category. The mode of action of such therapy is uncertain, but it may, by increasing the plasma volume, lead to a reduction in secretion of aldosterone and thereby cause diuresis. The disappearance of albuminuria which occasionally follows diuresis induced by a variety of therapeutic measures is one of the more mysterious features of the nephrotic syndrome. A variably effective way of reducing or abolishing proteinuria is by administration of the adrenal corticoids, especially prednisone. The beneficial action of the hormones appears to be due chiefly to a reduction of the permeability of the glomerulus to protein,[18] although they may also increase tubular reabsorption of albumin[18] and increase the volume of plasma by reducing secretion of endogenous aldosterone. The wide differences in clinical course and prognosis are probably due to differences in the nature and cause of the renal lesion. Further studies, microscopical and biochemical, may help to resolve some of the problems of pathogenesis.

PROGRESS IN MEDICAL RESEARCH

The Medical Research Council has recently published its 1957–8 annual report,[1] which, in its usual workmanlike and unostentatious way, combines an extraordinary amount of detailed information about the Council's activities and those who perform them, with its now customary survey of selected trends in research.

The Council's work continues to grow: in the year covered by the report 7 new research units were established, bringing the number up from 5 in 1938, and 39 in 1948, to 68 at the end of the period under review. Naturally its budget has increased: in the year ended March 31, 1958, Parliament provided a grant-in-aid of £3,032,889 (only 3.9% was spent on administration), as against £2,541,549 in the previous year.

It is worth noting that in addition to its research programme the Council has also advised the Government on a number of health problems,

[1] *Report of the Medical Research Council for the Year 1957-1958.* H.M.S.O., London. Price 13s. net.
[2] Sprat, Thomas, *History of the Royal Society of London*, 1667.

particularly those concerned with radiation. If one is to judge the full extent of the research done by the Council one has to turn to the end section of the report; here, in the separate accounts of the various units' activities, and in the 75-page list of the year's publications, are the bones of the Council's work. It is impossible in this short comment to do justice to all the activities described in the report. In recent years the Council has taken trouble to give the informed and interested, but non-specialist, reader a rather broader and less technical discussion of selected trends in research. Its intentions are honourable, but not always successfully carried out. Perhaps Thomas Sprat's advice[2] would help—"a close, naked, natural way of speaking; positive expressions; clear senses; a native easiness, bringing all things as near the Mathematical plainness as they can."

As in the past, the topics discussed in the report are divided between fundamental research and subjects of more clinical interest. Among the former are the section on the gracefully titled intracellular organelles; the account of the last eight years' work, mainly American, on cancer-producing viruses, which is being actively assessed and supplemented over here; the section on the new and highly sensitive techniques for the ultramicroscopic analysis of minute amounts of substances; and a section on mammalian fertilization in which the spermatozoon is shown to demonstrate the remarkable ingenuity that nature sometimes demands of its organisms.

The clinical topics discussed this year include diseases which affect literally millions of people—notably malaria, trachoma, and leprosy. Much research in the Gambia, where one child in three fails to reach adult life, has been devoted to assessing the effect of repeated malarial infection on the health of young African children. Some of the work on trachoma, the greatest single cause of blindness and impaired vision in the world, has also been carried out in the Council's Gambia laboratories. For the first time the disease has been induced experimentally in a blind human volunteer with virus cultivated in the laboratory. There are still 10 to 15 million lepers in the world. Unfortunately it is not yet possible to cultivate the leprosy bacillus or to transmit it to animals. Progress is, however, being made with experiments in rat leprosy, which closely resembles the human kind.

The Council has had a good many hard things said about it in recent months over its alleged lack of interest in psychiatric research, so that its account of work done on rehabilitating chronic schizophrenics is particularly opportune. There are some 37,600 patients, mostly schizophrenics, who have stayed in mental hospitals for more than 20 years. The Council's Social Psychiatry Research Unit has been working since 1954 on the social and psychological processes involved in retraining chronic schizophrenics. In a follow-up study of 229 schizophrenic men discharged from mental hospitals after an unbroken stay of at least two years, two out of three patients had succeeded in remaining out of hospital for at least a year, and, of these, two out of three were judged to be dealing adequately with life. Apart from the patient's clinical condition, the factors which were most likely to affect his resettlement were the type of home in which he stayed (he did least well with parents, and best with a landlady), and whether or not he succeeded in finding work. The whole project is psychiatric research of a very practical kind.

PENICILLINASE SHOCK

Largely owing to the efforts of R. M. Becker[1] the use of penicillinase for aborting reactions to penicillin has become a common practice, at least in the United States. This enzyme destroys penicillin rapidly, and a single intramuscular injection of it will eliminate the antibiotic from the blood.[2] While it does not act quickly enough to avail in the treatment of shock due to an injection of penicillin, it has been found valuable in ending reactions of the urticarial type, particularly when these are produced by long-acting preparations of penicillin which continue to be absorbed from a depot.

That penicillinase itself may cause a reaction has not hitherto been considered, for large numbers of patients have tolerated not only intramuscular but even intravenous injections of it. But recent case reports show this to be possible. S. Caputi[3] describes the case of a girl aged 5 who was given injections of procaine penicillin daily for five days for a severe sore throat after chicken-pox. A general urticaria appeared, which was thought to be a reaction to penicillin, and 800,000 units of penicillinase was injected intragluteally. Within a few minutes the child was acutely distressed, cyanosed, and dyspnoeic, with a weak and thready pulse, and a large area of swelling and redness appeared at the site of injection. This alarming condition was rapidly relieved by adrenaline, and treatment of the tonsillitis and urticaria had to be continued by other means. Coagulase-positive staphylococci were cultivated from the throat, and the author puts forward the novel idea that penicillinase formed by these organisms had produced sensitivity to this enzyme. Unfortunately no proof seems to have been obtained that this staphylococcus formed penicillinase; indeed, it is said to have been "sensitive" to penicillin, which no penicillinase-forming strain can rightly be said to be, though the statement that it was "very sensitive" to several other antibiotics leaves the significance of its behaviour in relation to penicillin in some doubt. This explanation seems improbable on two other grounds. Many patients with more severe and deep-seated infections by penicillinase-forming staphylococci must have been given penicillinase without such a result as this. Secondly, the penicillinases formed by different bacteria are not identical; therapeutic penicillinase is obtained from *Bacillus cereus*, and it would be surprising if this and the enzyme formed by a staphylococcus were antigenically indistinguishable. A. L. Hyman[4] has also described a similar immediate shock-like reaction, while M. Reisch[5] had two patients in whom the reaction was delayed and characterized by fever rather than shock. It is evidently too much to expect that a foreign protein

[1] Becker, R. M., *Ann. intern. Med.*, 1958, **48**, 1228.
[2] —— *New Engl. J. Med.*, 1956, **254**, 952.
[3] Caputi, S., ibid., 1959, **280**, 432.
[4] Hyman, A. L., *J. Amer. med. Ass.*, 1959, **169**, 593.
[5] Reisch, M., ibid., 1959, **169**, 594.

of this nature can be administered with impunity. What is surprising is that such effects have apparently not been seen before.

LEUCOTOMY FOR PAIN

For the treatment of severe and intractable pain there is no single remedy. As important as the cause of the pain—and there are numerous possible causes—are the reactions of the patient to it. In the past few years leucotomy has occasionally been undertaken for pain which will not yield to other methods, and a recent paper by A. Elithorn, E. Glithero, and E. Slater[1] is the latest and most careful study of its effects. They reported on 25 patients with pain, mainly of "neuralgic" type, and carefully followed them up by clinical interviews and by devising rating scales to assess social behaviour—a term that covered employment, family relationships, and community relationships (that is, leisure activities and social graces)—and the patient's reactions and his family's to the persisting symptoms.

Nine of the patients had extensive leucotomy operations and the rest more limited ones, three being unilateral. From earlier work Elithorn and his colleagues[2] had found that the leucotomy does not affect the actual perception of pain. There is nothing comparable, for example, to amblyopia (that is, loss of the usual emotional accompaniments of pain though the sensation itself is perceived) that is occasionally seen with brain lesions, nor is there any selective interference with the perception of autonomic or visceral pain. What is altered is the reaction of the patient to anticipated pain—in other words, the psychological reaction rather than the pain itself. The patients who obtained least benefit were those who were judged to have severe pain in the light of their distress when they were not aware of being observed and from the relatives' account of the way in which their activities were interfered with. There was also an interesting divergence between patients' views on how they were benefited and the assessment made from the rating scales. Only one-third of the patients said the pain was better, but three-quarters of them seemed improved so far as their social adaptation was concerned. Standard leucotomy produced better results in the patients' view than limited operations. The latter caused less personality change and therefore less effect on the pain, but the rating-scale assessments showed that they usually had a better effect than standard leucotomy.

Reports on the subject of intractable pain generally show how infrequently leucotomy is considered as a method of treatment likely to be of benefit.[3,4] The paper by Elithorn and his colleagues brings out the overwhelming importance of the correct assessment of the psychiatric picture as well as the cause and nature of the pain. Even so, it is difficult to find any clear indications enabling one to distinguish which patients are likely to benefit from leucotomy, since there are so many major variables to complicate the assessment. The patients in this series suffered from pains of diverse origin and duration, and their psychiatric disturbances were various, though depression was found in most of them. Several types of operation were performed and, as already mentioned, the outcome differed according to the method of assessment.

In recent years the numbers of leucotomies done for psychiatric disorders has been affected by two factors. The success of modified operations in relieving symptoms with minimal personality change has led to the operation being performed earlier on, before severe deterioration has set in. On the other hand, the general use of tranquillizers has certainly diminished the number of patients with acute psychoses who need operation. As to leucotomy for pain, the modified operation is of more doubtful value, and the judicious use of tranquillizers in addition to analgesics will avert the need for operation in some cases. Leucotomy for pain thus seems likely to remain a procedure that rarely needs to be undertaken, and then only after most careful assessment of the whole medical and psychiatric condition.

[1] Elithorn, A., Glithero, E., and Slater, E., *J. Neurol. Neurosurg. Psychiat.*, 1958, **21**, 249.
[2] Elithorn, A., Piercy, M. F., and Crosskey, M. A., ibid., 1955, **18**, 34.
[3] Botterell, E. H., Callaghan, J. C., and Jousse, A. T., *Proc. roy. Soc. Med.*, 1954, **47**, 281.
[4] Fischer-Williams, M., *Brit. med. J.*, 1956, **1**, 533.

DETERGENTS IN SEWAGE

There has been no detectable change in the average concentration of synthetic detergents in sewage, sewage effluent, and river water during the past two years. This fact is recorded in the second progress report[1] of the Standing Technical Committee on Synthetic Detergents. The difficulties which have arisen in recent years from the widespread use of synthetic detergents still persist.[2] In particular, foam is a cause of serious concern at sewage works and on certain rivers and canals. Fortunately the committee is able to record some encouraging results obtained at the Water Pollution Research Laboratory with a new type of synthetic detergent which is more readily broken down by the ordinary process of sewage treatment than the materials in current use. Preliminary measurements showed that effluents from treated sewage containing the new detergent foamed no more than the effluents containing no detergent at all. Other research on the foam nuisance is being carried out by the London County Council. By thoroughly aerating the "influent" to an activated sludge plant it is hoped to remove the surface-active material and so to keep it out of the Thames. A practical aid to research is the development of a standard method of comparing the foaming properties of effluents.[3]

In another investigation the toxicity of household detergents to fish was investigated. Trout were placed in water containing varying concentrations of detergents. About half of them died within twelve hours when exposed to a concentration of 12 parts per million of detergent. But the general conclusion was that in the concentrations likely to be present in British rivers detergent residues discharged with sewage effluents are unlikely to exert any appreciable toxic action on fish. Others besides trout fishermen may take some comfort from this.

[1] Ministry of Housing and Local Government, *Second Progress Report of the Standing Technical Committee on Synthetic Detergents*, 1959. H.M.S.O., London. Price 9d. net.
[2] See annotation, *Brit. med. J.*, 1956, **1**, 1536.
[3] Department of Scientific and Industrial Research, *Water Pollution Research 1958*, 1959. H.M.S.O., London. Price 7s. net.

OLD, CONFUSED, AND ILL

The increase in the proportion of elderly people in industrialized societies has yet to reach its peak, but the strain imposed by the mental frailties of old age on the community and present hospital resources is already serious. There is a disproportionate increase in mental hospital admission rates for older people, but it is not certain that this results from a real increase in mental disease. As the stigma of admission to a mental hospital lessens, so the demand for hospital care may increase. Processes of senile decay have, till recently, been all too easily blamed for any mental disorder in old age; but now, as the possibilities of treatment improve, the need for more precise diagnosis is apparent. The affective psychoses, paranoid states, and neuroses of the elderly already attract special notice; but the high proportion of cases in which a mental illness should be attributed in the elderly to metabolic, cardio-respiratory, or other disease outside the cerebrum deserves wider recognition both in hospital and general practice. For such reasons mental disorders of the elderly by no means warrant a uniformly poor prognosis. Many of them are benign and short-lived, especially when treatment is provided early. As Dr. P. D. Bedford[1] wrote in last week's *Journal*, confusional states in elderly people are potentially reversible and usually of good prognosis.

A recent report[2] from the World Health Organization analyses the sources of mental ill-health among the elderly, and mentions, particularly, low incomes, unenlightened retirement policies, and the social isolation of many old people because of deaths or migrations in the family. To these may be added, in time, the afflictions of general or cerebral diseases. The problem set by the mental frailties of old age can be solved only by a wide extension of facilities for care in the community, but these, as Miss Catherine Colwell and Dr. Felix Post point out in this week's *Journal* (page 214) are bound to be costly.

The Report of the W.H.O. committee advocates "geriatric guidance centres" based on hospitals, with out-patient and perhaps day-hospital facilities, a staff of social workers, and directed by physicians with a particular interest in the administrative, social, and mental problems of old age. It is suggested, too, that a quite small in-patient unit with full hospital facilities should suffice to deal with most of the acute psychiatric emergencies occurring in old people. Such units, if properly constituted and equipped with research facilities, would give much-needed prestige and stimulus to a specialty which has long been regarded as a poor relation of general medicine. Furthermore, the widely held view that nursing the elderly and mentally infirm is an inferior occupation may not be corrected until nurses are required to work in such departments as an integral part of their training, and thus to learn by experience that nursing the aged is a skilled and rewarding occupation.

[1] Bedford, P. D., *Brit. med. J.*, 1959, **2**, 185.
[2] Sixth Report of the Expert Committee on Mental Health, *Wld Hlth Org. techn. Rep. Ser.*, 1959, No. 171.

OVERSEAS RESEARCH COUNCIL

The establishment of an Overseas Research Council which would provide a central point to which Commonwealth Governments and research institutions could refer for advice and information was announced by Lord Home at the Commonwealth trade and economic conference in Montreal last year. The council has now taken shape, under the chairmanship of Dr. R. S. Aitken, vice-chancellor of Birmingham University, and Lord Hailsham gave details of it in the House of Lords on July 30. The United Kingdom Research Council, the Department of Scientific and Industrial Research, the Medical Research Council, and the Agricultural Research Council have agreed to give Commonwealth countries such help in research matters as they may require, wherever this can be done within the funds available. In addition to co-ordinating this assistance and formulating general policy, the Overseas Research Council will advise generally on United Kingdom co-operation in scientific research overseas. Besides Dr. Aitken, the other medical members of the council are Sir Charles Dodds, F.R.S., Sir Harold Himsworth, F.R.S., Dr. R. Lewthwaite, Professor J. McMichael, F.R.S., and Sir Solly Zuckerman, F.R.S.

An Order in Council has established a Privy Council Committee on Overseas Research, which will be advised by the Overseas Research Council, and which consists of the Lord President of the Council and the Secretaries of State for Commonwealth Relations, the Colonies, and Foreign Affairs.

POSTGRADUATE CONFERENCE AT R.C.P.

Last August the Royal College of Physicians of London held, most successfully, the first of a series of conferences arranged primarily to enable Fellows and Members of the College to hear about recent advances in certain specific branches of medicine. An account of the first conference, on "Anaemia and the Alimentary Tract," was given in this *Journal*.[1] Details of the second conference have now been announced: they were published in full in our advertisement pages on August 1 (p. 34). Intended for consultants in medicine or pathology, the conference will be held on November 13 and 14, 1959, and the subject will be "The Pathogenesis and Treatment of Occlusive Arterial Disease." Application should be made to the Registrar of the College not later than October 12. According to the provisional programme the four main subjects for discussion will be pathogenesis of occlusive arterial disease (chairman, Sir Robert Platt, Bt., P.R.C.P.); cerebral vascular disease (chairman, Dr. J. St. C. Elkington); coronary artery disease (chairman Dr. D. Evan Bedford); and peripheral vascular disease (chairman, Sir George Pickering). The College has done well to select a subject of such importance and topicality and to arrange for so many distinguished speakers to take part.

[1] *Brit. med. J.*, 1958, **2**, 301.

WASHINGTON CONFERENCE ON LIVE POLIOVIRUS VACCINES

[FROM A SPECIAL CORRESPONDENT]

A conference on live poliovirus vaccines was held under the auspices of the World Health Organization and the Pan-American Health Organization in Washington, D.C., from June 22 to 26. It was attended by 60 participants, most of whom had personal experience in the laboratory or in field trials of live attenuated poliovirus vaccines. The Sister Kenny Foundation had provided financial support for the conference.

Progress So Far

The first day was devoted to the general topic of the development, selection, and testing of attenuated poliovirus vaccines used so far. Professor G. W. A. DICK (Belfast) outlined some problems connected with the use of these vaccines, and stressed the difficulties which lay in deciding whether excreted viruses derived from the stools of those fed vaccine virus were detectably different from naturally occurring viruses, and also whether excreted viruses were either relatively or actually stable. He was followed by Professor A. B. SABIN (Cincinnati), who gave further details of the virus vaccines which he has developed, including information gathered since his paper published in the *British Medical Journal*, March 14, 1959. Professor Sabin described the newly demonstrated phenomenon of thermal sensitivity in the multiplication of attenuated viruses discovered by Drs. A. and M. Lwow (Paris). This lability contrasted with the ability of virulent viruses to multiply as well in cultures held at a temperature of 40–41° C. as at 37° C. Professor Sabin reaffirmed that excreted viruses, though showing some degree of reversion of neurotropic virulence for the monkey, nevertheless failed to exhibit any progressive change in such virulence. This was shown by tests on viruses excreted over periods of several days by the same person, and by tests carried out by Professor A. A. Smorodintsev (Leningrad), who had fed cultures of excreted viruses to children. As many as 10 successive "passages" in children had been made, and these had not shown any progressive rise in neurovirulence, although alteration from the original vaccine strain had been demonstrated.

Trials of Sabin's Vaccine Strains

These results were later described in detail by Professor Smorodintsev, when he also gave results on the field use of Sabin's vaccine strains in as many as 1½ million children in Latvia, Byelorussia, and Moldavia S.S.R. during an inter-epidemic period (March, 1959). These field trials embraced as many as 60 to 85% of children under 15 years of age in each of the several areas, and had resulted in a satisfactory development of antibodies to the three types of poliovirus without any clinical reaction or incident. Professor Sabin stressed the possible interference between different types of polioviruses when these were administered simultaneously. He had found similar interference with E.C.H.O., Coxsackie, and even adenovirus infection which inhibited or delayed infection by an administered vaccine. Such virus interference was particularly important in tropical or subtropical areas where a high rate of infection with enteroviruses was often found. Professor M. P. CHUMAKOV (Poliomyelitis Research Academy, Moscow) also described trials in the U.S.S.R., carried out independently of Professor Smorodintsev. A further 1½ million children had been immunized effectively and safely with Sabin's vaccine strains or with vaccines made from these strains. He had not found it necessary to give the three types separately, but gave a trivalent vaccine containing all three types, alone or after a previous administration of Type I vaccine.

Properties of Different Viruses

The properties of the attenuated viruses developed by Professor Sabin, Dr. H. Koprowski (Wistar Institute), and Dr. H. R. Cox (Lederle Laboratories) had been compared by Dr. R. MURRAY, of the Biological Standards Division of the National Institutes of Health (Bethesda). With standardized monkey inoculations by the intracerebral and intraspinal techniques, differences had been demonstrated between the three sets of viruses. In general, it was found that all the various agents produced lesions in the cord with or without paralysis after intraspinal inoculation of less virus than that required to produce infection of man by the oral route. By the intracerebral route, however, fewer or no effects were observed, and certain of the strains wer clearly less attenuated than others. Professor J. L. MELNICK (Baylor University, Houston, Texas) had also compared Professor Sabin's and Dr. Cox's viruses. He found considerable differences in the degree of neurovirulence of these sets of viruses in the monkey. The three Lederle viruses appeared to be somewhat more neurotropic and sometimes produced symptoms and lesions after intracerebral as well as intraspinal inoculation. Dr. V. J. CABASSO (Lederle Laboratories) then gave full details of the selection and manufacture of vaccines from these strains. Their field use in careful studies conducted by the Minnesota Board of Health was described later in the conference by Dr. R. N. BARR (Minneapolis). Five hundred and thirty-seven persons had received these vaccines in a series of carefully controlled studies on antibody responses and spread of viruses in a community of university staff. No ill effects had been observed which were attributable to the vaccines. The use of the Lederle strains of viruses combined together as a trivalent vaccine was also described by Dr. H. R. Cox (Lederle Laboratories) in over 500 employees of the laboratories, and by Dr. K. A. PREM (University of Minnesota) on a group of children and adults at the University of Minnesota, including some newborn babies and pregnant women. Excellent antibody responses were reported by both these workers, and no evidence of virus interference or of harmful clinical effects had been found.

Excreted Viruses

A series of studies on the properties of viruses excreted by those to whom attenuated vaccine had been given were reported. Dr. M. BENYESH-MELNICK (Baylor University, Houston, Texas) had examined the "marker" characters of viruses excreted by children in Mexico City after they had received Professor Sabin's vaccine. The "D+" character, which was the ability to grow in an acid culture medium, and the "T+" character, or ability to grow at 40° C., were both correlated with the property of neurovirulence for the monkey. Dr. Benyesh-Melnick had found that a high proportion of the viruses excreted by the children behaved similarly to virulent wild viruses in regard to the D and T characters. Direct inoculation of rectal swab material into monkeys had given evidence of virulence, and, though wild viruses undoubtedly occurred in the children from time to time, the number of viruses recovered from the children soon after vaccine-feeding was too great for the results to be explained as being due to extraneous agents. The reversion of the vaccine virus after passage through the alimentary tract to strains with a greater degree of neurotropic virulence had also been found by Dr. J. VERLINDE (Leyden) and Professor C. H. STUART-HARRIS (Sheffield) in small-scale trials of Dr. Sabin's strains. Dr. SVEN GARD (Sweden) also gave evidence of the immunizing effect within a family of a single feeding of the Type I strain of Koprowski (Chat) to one child in each family. Dr. Gard also found excreted viruses to possess the D+ character, though reversion of virulence was not present in the one strain tested.

Use of Vaccine During Epidemic

Two trials of attenuated viruses during or shortly before an epidemic of poliomyelitis were reported. That from Singapore was described by Dr. J. H. HALE (Newcastle), who had fed Sabin's Type II virus to 190,000 children during the progress of a Type I epidemic (*Journal*, June 20, 1959). The use of a heterologous antigen had permitted Dr. Hale to conclude that the vaccine virus had not induced cases of poliomyelitis, though the amount of protection conferred could not be estimated. The second trial was of Koprowski's

Chat (Type I) virus, which was given to 75,000 children in Leopoldville (Belgian Congo) shortly before cases of Type I poliomyelitis began to occur in 1958 (Dr. A. LEBRUN, Leopoldville). The epidemic did not appear to have been checked, but the vaccine was administered over a long period of time, and the serological findings suggested that only about 60% of the vaccinated subjects responded to the vaccine antigen. This trial indicated the grave complexity of the analysis of events following the use of an attenuated virus vaccine in a community about to be or already attacked by epidemic poliomyelitis due to a virus type similar to that contained in the vaccine. The difficulty of evaluating the protective effect of a live vaccine under such conditions was much greater than with inactivated vaccines. It was also agreed that the safety of the live vaccine could not readily be established in such circumstances.

Effect of Environment

A caution concerning the variable response of the host under different environmental conditions was voiced by Professor J. R. PAUL (New Haven), who described the results of feeding Sabin's Type I vaccine virus to a group of Mexican and Indian children in a remote community in Arizona. A heavy rate of infestation with enteroviruses was found in the children, and many strains of polioviruses were recovered from flies trapped in the vicinity. But only five children were infected by the vaccine virus, and no spread occurred. This high level of resistance to infection stressed the need for caution concerning the value of oral vaccines in certain types of population.

Field Trials

Field trials in Central America on a large scale were reported by Dr. H. ABAD-GOMEZ (Colombia) and Dr. M. L. BERRIOS (Nicaragua), who had used Lederle vaccines during an inter-epidemic period and shortly after a large Type II epidemic respectively. In Mexico City Dr. M. RAMOS-ALVAREZ had fed Sabin's vaccines; in Costa Rica Dr. J. M. QUIRCE Lederle vaccine; in Finland (Dr. N. OKER-BLOM) and in Poland (Dr. R. PRZESMYCHI) Koprowski's Chat Type I virus had been given. In all these countries a differing proportion of the children in the population had received the vaccines, the spread of virus to unvaccinated contacts had varied in extent, and the serological status before and after the vaccines also differed. The principle of the trials begun in the U.S.S.R., both by Professor SMORODINTSEV and by Professor CHUMAKOV, had been to give vaccine of Sabin type prepared in the U.S.S.R. during the winter, and to attempt to saturate a very high proportion of the susceptible population. The trials on a very large scale in the U.S.S.R. were quite recent (January to March, 1959), but, because of the complete absence of harmful effects, it had been decided to extend them even during the forthcoming poliomyelitis season. As many as 4½ million children had been immunized. In Czechoslovakia, where all children had already received two intradermal doses of Salk vaccine, feeding of Sabin's vaccine was made between December, 1958, and February, 1959, and nearly 150,000 children had now been immunized without incident.

Assessment of Results

It was agreed that assessment of the effects of these large-scale trials in different populations under varying social conditions was very difficult. Protection so far had been gauged by means of antibody responses, and these were encouraging. The need for constant surveillance was stressed. The difficulty of interpreting the origin of cases of poliomyelitis occurring after a vaccine programme had begun raised the need for some independent marker for identifying the strains used in the vaccine. A further problem lay in the difficulty of exclusion of a wild simian virus from the vaccine as prepared in monkey kidney cultures. It was stated that an unknown cytopathic agent had been demonstrated by one laboratory in a batch of vaccine already given to children. This was denied by other speakers, but the special risk which is inevitable with live vaccines containing no disinfectant cannot be denied. The discussion of the many papers presented during the conference left many people with an impression of a paradoxical situation. Lack of agreement concerning the degree of attenuation of the vaccines contrasted with the apparent lack of harmful effect in man. Variation in the amount of spread of infection to contacts and in the level of antibodies which were engendered suggested an explanation in terms of the population rather than the vaccine. The need for caution voiced by some contrasted with the confidence of those engaged in large-scale trials. It is clear that the experience now being gained should give an answer to some of the present problems in the not-too-far distant future.

BRITISH CONGRESS OF OBSTETRICS AND GYNAECOLOGY

[FROM A SPECIAL CORRESPONDENT]

The 15th British Congress of Obstetrics and Gynaecology was held at Cardiff from July 14 to 16 under the presidency of Professor G. I. STRACHAN. The congress was opened by Sir WILLIAM FLETCHER SHAW. The five main discussions were on the effects of obstetrical hazards on the development of the child, psychosomatic gynaecology, oestrogen metabolism, pelvic carcinoma, and the use of oxytocic drugs before the birth of the child.

Effects of Obstetrical Hazards on Child

In a guest paper introducing a symposium on this subject Dr. D. REID (Boston, Mass.) reviewed the obstetrical hazards which may threaten a baby, observing that inherited conditions and social factors are important. He stressed the recent work on infection of the foetus taking place through the umbilical cord itself, demonstrable at birth by immediate frozen sections, the importance of trained anaesthetists attending normal labours, and the damage which may result because of pelvi-cephalic disproportion which only becomes evident when labour is unexpectedly prolonged. This last he ascribed to abnormal shapes of the cavity and outlet, and he described how at the Boston Lying-in Hospital it was treated by a "double set-up" in preparation for either forceps delivery or caesarean section according to the findings when the patient was anaesthetized. Dr. C. M. DRILLIEN (Edinburgh) reported on a survey of 692 children born prematurely. Of those who were 3 lb. (1.4 kg.) or less at birth, and survived, the majority were found to be undersized and subject to a disproportionate amount of illness in their early years, with a large proportion of children who were mentally retarded and dull—21 and 60% respectively. Those above 4½ lb. (2 kg.) at birth grew up indistinguishable mentally and physically from their fellows born at term. Sir DUGALD BAIRD (Aberdeen) emphasized both the inherited and the environmental factors which cause an undersized baby of 5 lb. (2.3 kg.) born at full-time to be less favourably placed mentally and physically than a premature baby of 5 lb. delivered at 36 weeks. Prematurity was the major hazard to the newborn as a class, and Professor G. SHEDDEN ADAM (Brisbane) analysed its causes in 35,000 deliveries. Some 40 to 50% have to be described as "cause unknown," and he suggested that the psychogenic influences might be important.

In the afternoon Dr. J. B. DEWAR (Dumfries), president of the Edinburgh Obstetrical Society, was chairman. Dr. ALICE STEWART (Oxford) had taken part in social research involving surveys of pregnancies in large populations. One done in Northamptonshire showed that there was an increased risk of premature birth and more stillbirths and neonatal deaths in women who continued paid employment during pregnancy. Another investigation tested the incidence of obstetric complications, stillbirths, and neonatal deaths in certain physical types of mother, and it indicated that foetal death is more likely to occur if a

mother is short and fat than if she is tall and thin. Dr. M. S. FRASER (Aberdeen) investigated the neurological and psychological state of children from 6 to 11 years who had been asphyxiated at birth, excluding all premature babies. Using objective methods, he found that many of the children had been affected adversely both in personality and in the motor system. Professor J. WALKER (Dundee) opened the general discussion and spoke of the need for a department of human reproduction to study the wider implications of such problems. Mr. F. STABLER (Newcastle upon Tyne), Professor A. INGELMAN-SUNBERG (Stockholm), and Mr. J. A. CHALMERS (Worcester) participated.

Psychosomatic Gynaecology

Dr. D. O'NEILL (London) introduced the subject of illness due to stress giving rise to gynaecological symptoms. Mr. W. R. SLOAN, president of the Ulster Obstetrical Society, was in the chair. Dr. O'NEILL described stress as the wholly internal resistance of a person to an embarrassing environment. Emotional tension was the result, and not infrequently there might be gynaecological pain without demonstrable lesions. The menstrual cycle, too, was often affected, and this might occur in one of four ways: menorrhagia, period pain, irregularity, and amenorrhoea. Infertility was often due to spasm of the tubes due to emotional tension, and the spasm had been seen to relax under the *x*-ray screen when the patient was told a funny story. Another class of case showed frigidity and vaginismus. He advocated a stimulant form of treatment, but, to the general regret, gave no details. Mr. A. BOURNE (London) deplored the materialistic era of gynaecology which had resulted from the rise of surgery and scientific investigations, and which had shown itself by various -pexies and -ectomies. He was followed by Dr. J. W. JOHNSTONE (Melbourne), who gave a pictorial description of the sympathetic and hormonal control of the vascular endometrial bed, and particularly the way in which it can produce psychogenic amenorrhoea. He explained the importance of pin-pointing the time when menstrual periods ceased in order to diagnose the stress responsible. The removal of the cause was important; but the re-establishment of monthly bleeding by the well-known tablet method was a major part of the treatment because it gave such convincing support to psychotherapy. Dr. ELINOR BLACK (Winnipeg) discussed the menopause. In North America a doctor had to deal with a woman who had been led to expect serious trouble with her periods from her perusal of the women's popular papers, including *Esquire*. Oestrogen therapy was usually unnecessary, but she often saw it prolonged for years, and it sometimes produced serious trouble. Mr. J. B. BLAIKLEY (London) spoke on menorrhagia due to anxiety; and Mr. G. W. THEOBALD (Bradford) disagreed with previous speakers who had placed too much emphasis on psychological investigation, which was time-consuming, when quick treatment of a gynaecological condition by a minor operation would produce a speedy cure. He conceded that treatment by a psychiatrist, or by faith healers, or a visit to Lourdes might make the patient better, and possibly the last would cost least.

Oestrogen Metabolism

Mr. H. AGAR (North of England Obstetrical and Gynaecological Society) was in the chair when Sir CHARLES DODDS, F.R.S. (London), reviewed the early work on oestrogens which led to the synthesis of the many therapeutic substances now available. In a comprehensive introduction, he mentioned some of the applications of stilboestrol, including its use in stock rearing. The natural endocrine, oestrone, is rapidly destroyed in the body, whereas stilboestrol and other synthetic compounds are excreted largely unchanged. As 98% of beef cattle in the United States receive stilboestrol as implants or in their feed to give increased meat yields and hasten maturity, it was feared that the pastures would become highly charged with stilboestrol, which might have serious effects on other members of the animal kingdom. The fear was soon dispelled when it was established that soil bacteria rapidly destroy the oestrogens. Dr. J. B. BROWN (Edinburgh) described recent advances in synthesis, and particularly in the measurement of the excretion of urinary metabolites which indicates the amounts of oestrogenic hormones a patient is producing. Professor R. KELLAR showed how the use of these new methods of estimation had enabled the department in Edinburgh to study oestrogen metabolism. They found that urinary excretion of oestrogens during pregnancy increased several thousandfold, but in pre-eclampsia oestrogen excretion may be depressed. Professor B. S. TEN BERGE (Groningen) showed that in increasingly severe pre-eclampsia oestriol production in the placenta decreased and oestriol excretion in the urine fell until, at values lower than 10,000 gamma in 24 hours, death of the foetus was to be expected. He used the estimation method to know when he had to induce premature labour.

Pelvic Cancer

Professor H. J. DREW SMYTHE (Bristol), of the South-west of England Obstetrical and Gynaecological Society, was in the chair when Dr. H. TAYLOR (New York) described how at the Presbyterian Medical Center they were trying to conduct basic research into ovarian cystadenocarcinoma in clinical surroundings. It was a malignant growth in which inexplicable regression or rapid dissemination might occur, and so it was particularly suitable to attempt to correlate the clinical course with histological structure, chemical analysis of the cancer cells (particularly deoxyribonucleic acid), the ribonucleic acid content of the nucleolus, the measurement of oxygen consumption and lactic acid production of the cancer cells, and the tracing of radioactive ^{32}P in carcinomatous tissues.

Dr. W. G. COSBIE (Toronto), Professor B. W. WINDEYER (London), and Dr. C. J. L. THURGAR (Newcastle upon Tyne) all spoke of the improvement in the results of radiotherapy of carcinoma of the cervix uteri, and ascribed it to greater care in planning treatment and better technique. Super-voltage radiotherapy used on selected cases had some advantages; but here again technique was most important.

Place of Oxytocic Drugs Before Birth of Child

With Mr. S. DAVIDSON (Birmingham and Midland Society) in the chair, Mr. A. J. WRIGLEY (London) introduced the subject. He spoke as one who weighed over 10 lb. (4.5 kg.) at birth, whose mother had always been tall and thin, and who assured him that his father had never been out of work. He hoped the congress would condemn the use of intramuscular injections of oxytocic substances before delivery as highly dangerous, and never to be used now that the very dilute intravenous infusion ("pitocin" drip) had proved its value. Even the drip entailed definite risks unless cases were carefully chosen and good obstetrics prevailed. Amniotic embolism seemed to occur in these cases and was likely to prove fatal. Ruptured uteri had come to his notice. Professor J. CHASSAR MOIR (Oxford) advocated always making a graphic record of uterine action when an intravenous oxytocic drip was given, so that the clinician knew how the uterus was acting. He thought an ergometrine drip could be given if the foetus was known to be dead. Mr. G. W. THEOBALD (Bradford) advocated half a unit of pitocin or syntocinon added to 500 ml. of 5% glucose in distilled water, run in at 30 drops a minute. If this had no effect it should be followed by a second bottle containing one unit, and in one-tenth of his cases a third bottle containing two units was required. Rupturing the membranes was the primary method of induction of labour, and this was done first. He used the method extensively without any more supervision than that required by all women in labour. Professor H. M. CAREY (Auckland) gave his results and showed a film. He suggested that many of Mr. Wrigley's troubles were due to his patients being given a pitocin drip without having the membranes ruptured first. He now preferred to rupture the forewaters.

New Appliances

UTILITY SPLINT FOR FRACTURED METACARPAL

Dr. G. T. ASHLEY, lecturer in anatomy, Manchester University, writes: The injury sustained in Australia by the England cricketer Ramon Subba Row (fracture of a metacarpal bone) prompts me to record a personal experience which stimulated me to improvise a splint for an injury of this nature. Though having a limited use, such a splint could prove invaluable in certain emergencies.

A few years ago I sustained a fracture of the fifth metacarpal bone of my right hand. The injury occurred at net practice some 40 hours before I was due to play in a match in which I was to keep wicket. After several experiments I devised a splint which could be readily made and easily applied or removed, and which would permit me

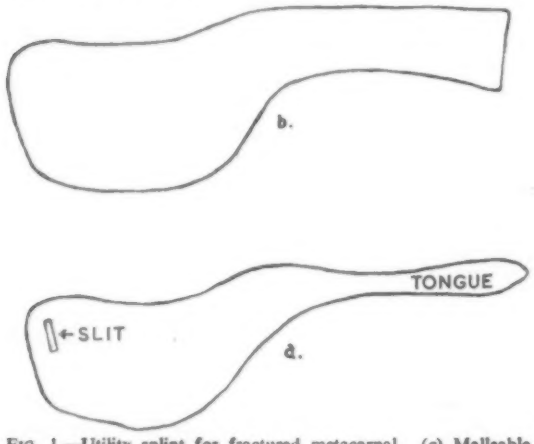

FIG. 1.—Utility splint for fractured metacarpal. (*a*) Malleable metal splint; (*b*) Felt protector.

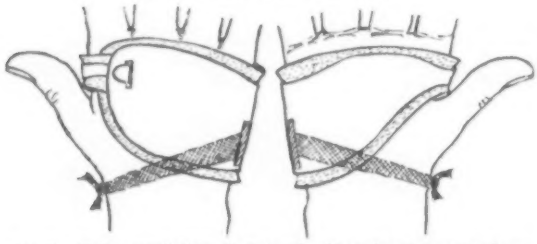

FIG. 2.—Splint applied to right hand. Dorsal and ventral views.

both to wear wicket-keeping gloves and to hold a bat. Wearing this splint, on the second day after sustaining the injury, I succeeded in keeping the byes down to 2 out of a total of 192 and in batting for a period of 40 minutes. This was achieved without any serious discomfort.

Thereafter, for a period of three weeks, I wore the splint only when engaged in rigorous manual work. For ordinary purposes such as writing, dissecting, blackboard drawing, etc., it sufficed for me to tie the little finger to the ring-finger with cotton thread; otherwise the weight of the little finger was sufficient to cause aching at the fracture site, and the finger assumed an abducted position. In this position the tip of the finger seemed to catch against some object or other on every conceivable occasion. There was no significant loss of function. The bone healed with minimal angulation, and has given me no further trouble.

Details of Splint.—Requirements: one piece of ¼-in. (0.6-cm.) felt about 12 by 5 in. (30 by 12.5 cm.) and one piece of malleable metal (copper or white metal) about 12 by 4 by 1/16 in. (30 by 10 by 0.16 cm.). By direct application

(*Continued at foot of next column*)

(*Continued from preceding column*)

make a paper pattern from the hand of the patient, and from this pattern cut the splint from the piece of malleable metal (Fig. 1, a). Cut a slightly larger, but similarly shaped, protector from the piece of felt (Fig. 1, b). Fold the felt protector around the palm and hold it there whilst the metal splint is bent into position, the "tongue" being threaded through the slit and then bent back on itself (Fig. 2). Finally, a length of gauze bandage is strapped to the ulnar side of the metal splint and tied over the "snuff-box," to prevent the splint from slipping.

Such a splint has the following advantages: it is inexpensive and easily made; it interferes to a minimal degree with function; it may be removed by the patient as occasion demands; it may be replaced by the patient as required; it gives sufficient confidence and protection to enable a sportsman to play in an emergency; it could render similar service for any artisan using pick or shovel; and on the single occasion when it was used it enabled near-perfect repair of the fracture to occur in the short period of three weeks.

Warning.—It would, of course, be unwise to recommend indiscriminate use of this splint. It was found to be perfectly satisfactory for the case reported—a simple transverse fracture of the shaft of the fifth metacarpal without displacement. It is recognized that each case should be treated on its merits.

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Etisul (Imperial Chemical Industries).—This is diethyl dithiol*iso*phthalate, or E.T.I.P., available for clinical trial as 5 g. in 7-g. tubes of cream.

Ethyl mercaptan and its derivatives have been shown to be inhibitory to intracellular tubercle bacilli in culture. The leprosy bacillus cannot be cultured or maintained in animals, and so drugs for treatment of infection with this organism have to be selected empirically and tested on man. E.T.I.P., or etisul, a thiol ester, is considered to be one of the most promising derivatives of ethyl mercaptan. An oily yellow liquid, it has proved most effective against tubercle infections in mice when given percutaneously or subcutaneously. When so given the drug is absorbed quickly and completely. A 75% concentration in magnesium stearate paste given by inunction significantly prolonged the lives of tubercle-infected mice.

Some 100 patients with leprosy have now been given E.T.I.P. either orally or by inunction. The reported results, both bacteriological and clinical, of treatment by the latter method have been remarkably good in nearly all cases. They have been assessed against results obtained on oral treatment with diaminodiphenyl sulphone—the present standard treatment for leprosy. But these good and rapid responses were evident only during the first few months of E.T.I.P. treatment; thereafter there was evidence of the development of increasing resistance to the drug. Nevertheless, given by inunction for the first eight to twelve weeks of treatment, together with and sustained thereafter by the standard diaminodiphenyl sulphone treatment, E.T.I.P. promises a more speedy and effective control of clinical leprosy than has hitherto been achieved. There is no evidence of interference with the drug's action as a result of simultaneous treatment with other drugs.

The dosage at present advocated is 3 to 6 ml. by inunction twice weekly for two to three months. There have been no toxic side-effects to date, and there are no contraindications to the use of E.T.I.P. other than the ultimate development of resistance to it. The psychological benefits from this mode of administration are considerable in a disease such as leprosy, with its obvious skin lesions. The disadvantage from which the drug suffers is its unpleasant, pervasive, and persistent odour; in pastes or creams this can to some extent be masked by strong perfumes.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Long-term Anticoagulant Therapy

SIR,—Professor J. McMichael (*Journal*, April 11, p. 970) and Drs. G. E. Honey and S. C. Truelove (*Journal*, May 16, p. 1299) are right to emphasize the possibility that observer bias may affect the results in trials such as the one reported by us (*Journal*, March 28, p. 803), where the need to adjust dosage makes it impossible to keep the physician in ignorance of the treatment given. Such bias is unlikely to have affected the difference in the mortality rates and, although this does not satisfy conventional limits of statistical significance, the results could have arisen by chance only in about 1 in 10 such trials. Our aim has been to present the results, using alternative indices, of the effects of treatment (of which Drs. Honey and Truelove have selected one) so that readers could sense the consistency of the evidence which we believe to be important and so that some of the difficulties in interpretation in long-term trials could be pointed out.

The same rules could not be applied for reinfarction as for admission to the trial, because Q-wave evidence may persist after severe infarction and because, as mentioned in the report, insistence on Q-wave evidence even for a first infarct excludes about two-thirds of the cases severe enough to be admitted to hospital and accepted as infarcts on clinical and other electrocardiographic grounds. Instead, clinicians were asked to categorize the evidence for reinfarction, both clinical and electrocardiographic, either as good or otherwise. Of the reinfarctions which did not cause death the distribution of ratings given to the clinical evidence and to the electrocardiographic evidence showed no significant difference between the two treatment groups. The trial design laid down that, after reinfarction, patients should be returned to their original treatment groups after 28–42 days of treatment by phenindione in high dosage unless their condition had deteriorated. Drs. Honey and Truelove may be correct in supposing that physicians were biased in their recognition of such deterioration and in favour of withdrawing their patients from the lower dosage regime particularly after repeated infarction. Had this happened, however, the low dosage series should contain correspondingly less severely ill patients and the ensuing follow-up would have been biased against the high dosage regime. The inclusion of such withdrawals in one of the alternative statements of results was thus essential.

As Professor McMichael says, there is certainly no justification for the arbitrary selection of data from particular age or sex groups to suit a specific argument. The division of results according to age and sex, however, follows both sensible convention and *a priori* reasoning based on previous experience of the differing natural history and prognosis of infarction in the young male and the older patients of both sexes.

Without discussing the generality of Professor McMichael's statement that the patients at greatest risk of death or recurrence form the most sensitive group for clinical trials, one might point out that, as Table VIII of our report showed, the effect of treatment seemed to be most marked among males with a history of previous infarction for whom the rate of recurrence or death in the low dosage group was greatest.

Professor McMichael expresses his disappointment that the trial has not given more decisive results. It seems worth while relating that at its meeting on March 11, 1958, the Working Party received an interim report on the trial up to October, 1957, the patients having been admitted at any time after November, 1955. The position as regards deaths in the low dosage and high dosage series at that time is shown in Table I.

TABLE I.—*The Position as Assessed up to October, 1957*

	Number of Previous Infarcts on Admission							
	I		II		III		Total	
	Low Dosage	High Dosage	Low Dosage	High Dosage	Low Dosage	High Dosage	Low Dosage	High Dosage
Total no. of patients ..	123	122	21	24	5	6	149	152
Deaths ..	18	5	1	—	2	—	21	5
Deaths per cent. ..	14·6	4·1	4·8	—	40·0	—	14·1	3·3

The differences in the death rate were statistically significant. Moreover, the two treatment groups showed suggestive differences in the same direction in the rate of reinfarction and in the various indices of working capacity. Because it seemed clear to the Working Party at that time that continuing high dosage of phenindione apparently saved life in the first few months of treatment, they considered that with this knowledge they were not justified in admitting new patients to the trial, though the patients already admitted were retained on the treatment as begun. In the final analysis, which included additional patients admitted to the trial between October, 1957, and March, 1958, the differences in mortality rate were less definite than had originally appeared. Table II shows that in the last year of the study there was both a reversal of results in the first six months and an accumulation of deaths thereafter. The Working Party has of course shared Professor McMichael's disappointment that the results were less decisive than was hoped. But they would like it to be realized that, if they erred, they erred out of consideration for their patients.

TABLE II.—*Time Distribution of Deaths*

Time Since Admission	Low Dosage Series			High Dosage Series		
	1956	1957	1958	1956	1957	1958
<3 months ..	5	8	1	—	4	2
3–	2	3	2	—	1	5
6–	—	3	1	—	1	2
9–	—	—	—	—	—	3
12–	—	3	2	—	—	1
24+	—	—	1	—	—	3
	7	17	7	—	6	16

Our remarks on the assessment of results in the second and later years of a long-term study apply quite generally and they were not intended to plead the specific case of anticoagulants. If any method of treatment either delays or prevents the death of the more seriously ill patients during the first year of follow-up, the two treatment groups which were alike at the beginning of the year are inevitably biased at its end in a way which favours the control group of selected survivors. In each successive year, then, the comparisons between the two groups become progressively more difficult to interpret, and the summation of results over several years may, as in this study, understate the value of a partially effective treatment without denying it. We understand that trials are under way in Denmark, Norway, and the United States. If their results agree with Bjerkelund's[1] and our own, then perhaps they may help to remove legitimate doubts raised by the failure of the available comparisons to be quite decisive.

We see no reason to depart from the rather cautious conclusions of our report, which may be quoted: "The conclusions derived from this preliminary analysis must be tentative. The strict criteria adopted in this study exclude about two-thirds of patients admitted to hospital, diagnosed and treated as cases of cardiac

infarction. Our conclusions apply only to the type of patient selected. But it appears that phenindione administered continuously in the conditions of this trial can make a useful, if limited, contribution in the after-care of patients who have recovered from the acute phase of myocardial infarction."—We are, etc.,

WORKING PARTY OF THE MEDICAL RESEARCH COUNCIL ON ANTICOAGULANT THERAPY IN CORONARY THROMBOSIS.*

London, S.W.1.

REFERENCE

1 Bjerkelund, C. J., *Acta med. scand.*, 1957, **158**, suppl. 330.

*The members of the Working Party were Professor Sir George Pickering (Chairman), Professor W. M. Arnott, Dr. R. Briggs, Professor H. W. Fullerton, Dr. A. R. Gilchrist, Professor R. B. Hunter, Dr. D. D. Reid, Dr. P. Wood, Dr. J. H. Wright, and Dr. A. S. Douglas (Secretary).

Whither Medicine ?

SIR,—One looks forward weekly to reading your leading articles, keeping one *au fait* with modern trends, and up to date with digests of literature in all manner of subjects in which one has not a primary interest. I am a little disturbed, however, at the annotation on ergotamine treatment of migraine (*Journal*, July 18, p. 69), though realizing it is mainly a warning about the use and misuse of this drug. The first paragraph suggests that the exclusion of an organic basis should go so far as to eliminate internal carotid thrombosis or anomalies of the circle of Willis, and that this is essential before diagnosing idiopathic migraine. I only hope I am not reading too much into this, but the idea terrifies me. The second paragraph recommends the eradication of any precipitating factors (doubtful ones in sooth), and "to see that the patient regulates his life to a steady pattern, free from severe anxieties and stress." Really, must one use such a time-worn cliché ? How does one do it ? Does it mean giving the patient £3,000 a year, a harmonious spouse, and beautiful, placid children, interesting but steady work, and of course the "Telly" ? Isn't it time to realize that the stress that is important in disease is the inner stress, which so few of us are trained to elicit or understand ? It is part of the same idea as excluding organic disease when the largest single factor in ill-health is probably not organic at all. It is high time the medical educationist should realize that man's mental and physical development occur in a continuously changing social *milieu* of which he is part, and that doctors should be trained to see the whole of man in this way, and to be able to take a medical history free from bias towards organic or functional aspects. Human medicine is for human beings.—I am, etc.,

London, W.1. HUGH GAINSBOROUGH.

Acroparaesthesia and the Carpal Tunnel

SIR,—This subject is certainly ripe to be discussed again. You mention (*Journal*, May 9, p. 1230) Dr. Ritchie Russell's important point that the tendency is to look for pathological abnormality at one level only of the peripheral nerve. I agree that one should not become too preoccupied with small stretches only of the axon and that more attention should be paid to the unity of the neurone, but I think that Dr. Russell, in his turn, and also some of your correspondents (*Journal*, June 6, p. 1472 ; June 13, pp. 1527 and 1528), may be giving too much emphasis to *pathology* at levels of the nerve other than where it is most obviously affected.

The borderline between pathology and *physiology* must in some of these cases be narrow, for many degrees of compression are possible, and whatever may be the altered state occurring within the nerve the threshold necessary for the production of symptoms is not commonly reached. The nerves of the upper limb do not all appear to be very efficiently protected, and there may well be embarrassment to some of their constituent axons at various levels which is not necessarily pathological. I think that this is likely not only during everyday activity but also during sleep, when muscle tone is relaxed and the axons, or their blood supply, are more subject to deformation by the weight of the recumbent body, and when perhaps the vasodilatation suggested by Professor F. A. R. Stammers (*Journal*, June 6, p. 1472) aggravates matters. This symptomless, *quasi-physiological* compression, friction, or stretching may occur at any of the numerous sites that have been incriminated individually. Pathological changes at any of these points, or in the intervertebral disks, may result in further embarrassment sufficient then to produce symptoms, and vascular insufficiency may also play a part—perhaps the major part—in many instances of "compression."

I suggest that there may sometimes be a cumulation of the various forces acting on the nerve, reaching the threshold required to produce symptoms. I have considered this possibility ever since I saw a girl with syringomyelia where the cavitation of the cord had at first affected the neurones destined to form C.8 and T.1 nerves. By then the diagnosis had become clear, but four and a half years earlier she had had weakness of the little and then of the ring finger (and, later, hyperthenar wasting), and a dull, tingling ache down the medial border of the forearm as far as the wrist. After she had had these symptoms for two years, a diagnosis of "scalenus anticus syndrome" had been made, and this appeared proved when the symptoms (except the wasting) were entirely relieved by scalenotomy, and remained so for more than two years subsequently.[1]

The almost unbelievable success of anterior carpal ligament division, even when there is pain right up the arm, and sometimes even when there is a cervical rib or spondylosis, makes me wonder whether this operation is not similarly non-specific in its action in some cases. "Make haste to use your new remedies," said Samuel Gee, "before they lose the power of working miracles." Orthopaedic surgeons and others have now made haste and hay, and the sun still shines on this little miracle ; while some neurosurgeons have turned orthopaedic and are hammering away at the cervical spine in the vicinity of the other ends of the same neurones.

And may there not also be an equally thin borderline between pathology and *anatomy* in the case of the median nerve in its relation to the anterior carpal ligament ? Some readers will recall the polemics between Professor H. A. Harris[2] and Mr. Dickson Wright[3] that enlivened the inauguration of the carpal tunnel operation. The argument was whether swelling of the median nerve in this situation is anatomical or pathological. Perhaps it is both, for it seems unlikely that the anatomical (? quasi-anatomical) subjects with this "pseudoneuroma" which were examined by Cloquet, Quain, and Harris all had the carpal tunnel syndrome ; and it is a fact that by no means all median nerves that are successfully "decompressed" show any very remarkable appearance.

Finally, it is still possible also, I suppose, that fluctuating humoral factors may play a part in facilitating the appearance of paraesthesiae in response to nerve compression or ischaemia that might ordinarily be symptomless. A patient of mine, during a recent spell of acroparaesthesia, also had sciatica. Roaf[4] raised the possibility of dietetic deficiency, and there do appear to be days when one seems to be abnormally susceptible to mechanisms that produce paraesthesiae : when contact for an accustomed time with a familiar lavatory seat produces sciatic paraesthesiae that are not usually experienced, and when a normally comfortable size of

rubber glove causes paraesthesiae in the fingers (usually in median nerve territory) during the performance of a routine operation. But speculation, and perhaps imagination, have been carried quite far enough.—I am, etc.,

Manchester, 13. JOHN POTTER.

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Iproniazid in Depressive Syndromes

SIR,—In their paper on iproniazid in depressive syndromes (*Journal*, June 13, p. 1491) Dr. E. D. West and Dr. P. J. Dally indicated that they initially considered a controlled evaluation; they were dissuaded by the difficulty in obtaining a homogeneous basic group and the fact that iproniazid has easily recognized side-effects. Both of these difficulties are inherent in any controlled evaluation of any active drug used in psychiatry. This is no argument for avoiding the use of a placebo group, and certainly will not give a clinical study the weight of carefully controlled research.

Their paper actually provides one answer to their dilemma in selecting a homogeneous group. The clinical results indicated that iproniazid appeared to benefit the "atypical or hysterical" depressions, particularly patients with previous "relatively good personalities." Such a basic group should be homogeneous enough. The other difficulty, that of side-effects giving the game away, is not in fact so marked in iproniazid as when using the phenothiazines. A placebo group, however inadequate the disguise, is better than none, and side-effects have a remarkable propensity for occurring in inactive placebo groups. The perfect answer is to use an active placebo group as well as an inactive.

That iproniazid appeared to benefit the patients most susceptible to placebo suggestion indicates the worth of an uncontrolled evaluation. The extreme toxicity of iproniazid cannot be ignored. A patient is better off with an "atypical depression" and an intact liver than an intact personality with acute hepatic failure.—I am, etc.,

P. H. GWYNNE.

Columbus Psychiatric Institute and Hospital,
Ohio, U.S.A.

Recovery from Cardiac Arrest

SIR,—We describe below a case of cardiac arrest which endorses the view of Blair, Irvine, and Taylor[1] that there may be a surprising degree of recovery from the neurological sequelae of such an incident.

W. C., 66 years, retired (formerly a labourer), had a routine herniorrhaphy performed in hospital. He was given 0.5 g. thiopentone, nitrous oxide, oxygen, and cyclopropane, and 80 mg. gallamine triethiodide. The muscle tone returned to normal by the end of the operation, which was completed in less than 30 minutes. Four hours afterwards the patient's pulse was recorded as normal by a nurse, who, a moment later, was impressed by a rapid onset of pallor, disappearance of the pulse, and the fact that the patient had stopped breathing. Examination by one of us hastily summoned to the ward revealed a cadaveric appearance, with no heart sounds and no pulsation in major vessels. There was no evidence of regurgitation of gastric contents. A diagnosis of cardiac arrest of unknown aetiology was made and artificial respiration was begun while the emergency tray was being brought.

Two ml. nikethamide was injected into the cavity of the left ventricle, the myocardium being needled twice in this procedure, and artificial respiration continued until an endotracheal tube had been passed and oxygen therapy begun. By the time the thoracotomy tray had been brought from the operating theatre, a strong radial pulse had returned. We estimate that at least four minutes elapsed until the circulation was restarted.

At this point the patient was completely flaccid, with dilated pupils. Within 15 minutes rigidity of all limbs developed. The patient's subsequent progress is summarized in the Table below. Two and a half hours after the incident the full clinical picture of decerebrate rigidity was present, but on examination five hours later the tone and position of the limbs had almost returned to normal. Fifteen hours after the cardiac arrest the patient was able to sit up in bed, read a newspaper, and talk, although slight slurring of his speech was present. His memory was not impaired. He appeared completely normal by the following day. There was no defect in the visual fields on detailed examination. E.C.G. examination 15 minutes after the cardiac arrest showed no abnormality. However, serial E.C.G.s suggested that the patient had sustained a small subendocardial infarct as a result of coronary artery thrombosis. This presumably caused cardiac arrest probably following ventricular fibrillation.

Much has been written on cardiac arrest in the operating theatre,[1 2] but the standard of preparedness in the wards is not so high as in the theatre. This case shows that, when it presents as a medical complication in the post-operative state, much good can be done by artificial respiration, endotracheal oxygen, and needling of the myocardium, as long as these measures do not delay the performance of the more direct surgical measure, cardiac massage. In this instance the heart was probably restarted by the stimulation of the myocardium by the needle. The injection into the chamber of a non-contracting heart can have played no part.

The complete recovery from neurological damage is the outstanding feature of this case. The degree of neurological damage must bear some relation to the duration of arrest of the circulation and consequent anoxia. Most observers have stated that a period of 100 seconds to 2 minutes represents a crucial time for survival of the nervous tissue of the human brain.[3] Krainer[4] lists very much longer survival times for the dog—cortical centre 5 minutes, vasomotor and respiratory centre 15–30 minutes. He believes that the values for man are too low. We agree with this because of our experience in this case and feel that Steegman's

Time	Pulse	B.P. (mm. Hg)	Temp. (°F.)	Comment	Deep Reflexes	Pupils
0	Absent	Unrecordable		Flaccid	Absent	Dilated
15 min.	90	120/70	99	Spastic ++ in all four limbs	Equivocal	Small, reacting to light
2½ hr.	90	130/70	98·4	Appearance of decerebrate rigidity; extensor plantars	,,	,, equal, reacting to light
7½ ,,	90	130/70	98·4	Upper limbs no longer flexed; tone + but lessening →normal	Present	,, ,, ,, ,, ,,
9 ,,	90	130/70	98·4	Oxygen therapy discontinued; becoming conscious now	,,	
15 ,,	84	130/70	99	Reacting to environment, speaking; speech slurred a little. Memory—normal	,,	Normal
24 ,,	82	130/70	98·8	Normal	,,	,,

values[3] should be doubled. This would emphasize the importance of attempts to restart the circulation even up to 5 minutes after the onset of cardiac arrest. This case illustrates that a successful outcome may be brought about by simple measures when facilities for thoracotomy are not immediately available.—We are, etc.,

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A. N. SMITH.

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Survival after Cardiac Arrest

SIR,—We think that Mr. C. A. B. Clemetson should be congratulated on his candour in publishing the article on "Survival After Cardiac Arrest" (*Journal*, July 4, p. 14). We do feel, however, that in the sequence of events which led to the incident of cardiac arrest there were a number of avoidable factors. Though these practices may still be widely indulged in, we feel that they do not accord with modern obstetrical concepts; and we feel it would be of value to draw attention to the following points:

(1) We would suggest that if possible, and especially in a nursing-home and when the delivery is conducted by a doctor, intravenous and/or intramuscular ergometrine should be given routinely in the interests of prophylactic reduction of postpartum haemorrhage.

(2) Most would agree that ergometrine should certainly be given in the third stage, in the presence of a brisk loss of 40 oz. (1.1 litres).

(3) In most centres it is considered that the practice of allowing the placenta to remain *in situ* for one hour without taking steps for its removal (even in the absence of haemorrhage) is inviting trouble. Steps should be taken after 40 minutes, allowing time for premedication, etc., so that its eventual removal can be effected at the end of one hour.

(4) Present-day teaching condemns the giving of morphine subcutaneously to shocked patients, since it is not absorbed by a collapsed circulation. Recent research would suggest that its administration in shock is contraindicated if pain is absent.

(5) It must be universally accepted now that a vital part of antenatal care should be the investigation of the patient's blood group and Rhesus factor. If this is done, compatible blood can be made available much more readily.

(6) We do not agree that a blood pressure cannot be taken on a "drip" arm, as the vein is occluded for a matter of seconds only; the information so derived is most important. Clinical impressions are not always reliable.

(7) Chloroform, few would deny, is a dangerous anaesthetic agent. Many people would condemn its use at all, but if employed it must be only by anaesthetists who know what they are about; and anyway it is not suitable in recently resuscitated patients, since it produces a marked circulatory depression. The development of laryngeal spasm is likely to be due to its administration in an initially strong and sudden concentration. To persist with its use in the presence of stridor (*ergo* anoxia) is most unwise. It is just in the induction of such an uneven anaesthetic in a frightened and exhausted patient that chloroform is most dangerous and the chances of cardiac arrest are greatest. Furthermore, the premedication before a chloroform anaesthesia with ¼ gr. morphine (22 mg.) is not to be recommended.

(8) It is generally felt nowadays that the administration of nikethamide intramuscularly after cessation of heart beat is patently a waste of time and has no place in cardiac resuscitation.

(9) The modern treatment of cardiac arrest dictates that there must be an almost reflex sequence of therapeutic steps: "confirmation of arrest—ventilation and cardiac massage." Artificial respiration cannot be delayed; certainly a heart will "tend to fail" if it pumps round reduced haemoglobin for the best part of ten minutes. A 1/1,000 solution of adrenaline would be better substituted by 10 litres of oxygen/minute.

(10) We would suggest that artificial respiration by external pressure is of little value in a patient with an open chest. Without proper equipment mouth-to-mouth inflation is the only satisfactory method.

(11) We were a little surprised at the anaesthetic technique employed. In a patient's house the "rag and bottle" may be the only available equipment, but in a nursing-home with proper apparatus there seems little good reason why it should not always be available, for we feel that, if it is not kept available, then emergencies such as removal of retained placenta should be only dealt with by fully equipped and competent Flying Squads.

If to many it seems that we are merely stating the obvious and generally accepted truths, we feel that they are principles which apparently need repeated emphasis; they include some of the most basic principles of accepted modern obstetric and anaesthetic practice to which one *must* strictly adhere.—We are, etc.,

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London, W.2.

H. SAVERY.

Brighton.

Hand-operated Resuscitator

SIR,—May we answer Dr. C. D. Sanders's criticism of our resuscitator (*Journal*, July 18, p. 73)—namely, that the facepiece mount should be a straightforward British push-on attachment so that a standard anaesthetic mask could be substituted in the event of the resuscitator facepiece perishing? As we pointed out in our article, all the rubber parts are "of high quality, with a life of at least ten years." What is more, the mask is designed in such a way that even in the event of the rubber ageing the resuscitator would still work satisfactorily.

The connexions are the standard ones agreed to for respiratory work by countries of the North Atlantic Treaty Organization. The use of British Standard anaesthetic fittings was deliberately avoided lest people were tempted to do the very thing Dr. Saunders suggests—that is, to use the resuscitator with endotracheal intubation or for prolonged hospital resuscitation. This device was not designed as a piece of hospital equipment, but primarily for first-aid use in the field. For such emergencies it is unlikely that anaesthetic equipment, including facepieces, would be available.—We are, etc.,

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C. G. TROTMAN.
H. W. WHITCHER.

Chemical Defence Experimental
Establishment, Porton Down.

B.C.G. Vaccination

SIR,—Your leading article "For and Against B.C.G." (*Journal*, June 6, p. 1460) provides a welcome breath of fresh air after the copious exhaust fumes with which seventeen space occupiers filled seven pages (pp. 1423–30). Burning their methane with an intensity sufficient to twist steel, your contributors have left themselves without enough light to see what their nearby neighbours have been up and doing. Little wonder that Heimbeck's

nurses[1] and Dahlström and Difs's conscripts[2] are ignored when reports from Chicago (Neiman and Loewinsohn[3]; Rosenthal[4]) of similar surveys, as close to controlled trials as can be attained outside concentration camps, go unnoticed. Only contortionists would coolly accept Levine's[5] results and brazenly reject those of Aronson *et al.*[6] and the Medical Research Council,[7] alter the standards of differentiation between primary and re-infection from serial skin-testing or radiography as recommended rightly on one page to bacteriological findings—no less—which are demanded on another, or feel self-satisfied with an expensive expectant policy such as serial tuberculin testing in the face of a "backlog of 56,000,000 persons harbouring tubercle bacilli." And since no untruth is half so effective as a half-truth, it is disconcerting to find experiments of Petroff *et al.*[8] quoted without comment or Ström's[9] demonstration of the immune response to reinfection consequent upon B.C.G. inoculation ignored, although his earlier work[10] receives notice.

It is an open secret that nowadays advanced physicists ($64,000 variety) can be found without difficulty in the U.S.A. among boys of 4 years, and that teen-agers there are mature citizens of the world, but it is surprising to learn that infants and adolescents have not existed in the States since the Wall Street crash. How else can we, aware of the work of Price[11] and of Bentley *et al.*[12] amongst others, explain the invariable benignity of natural primary tuberculous infection reported by Myers *et al.* in 1935[13], upon which the whole case against B.C.G. vaccination is built ?—I am, etc.,

Dublin. C. S. BREATHNACH.

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Intermediate Megaloblasts

SIR,—May we comment on your annotation (*Journal*, January 10, p. 105) and on Dr. D. L. Mollin's letter (January 31, p. 302) ?

In 1938 Fairley, Bromfield, Foy, and Kondi[1] reported intermediate megaloblasts from cases of megaloblastic anaemia occurring in Macedonia. Since then these cells have been described by many Continental workers as "megaloblastoids" or "megaloblastiform cells" and their significance commented upon (Heilmeyer and Schöner,[2] Bessis,[3] Guglielmo,[4], Zuelzer,[5] and Heilmeyer and Begemann[6]). Altmann and Murray[7] described them from cases of kwashiorkor with haemoglobins down to 5 g./100 ml. Cases with low haemoglobins have also been described from India and Africa (Ramalingaswami and Menon,[8] Foy and Kondi[9 10 11 12]).

In these countries it is our experience that there is little relation between the degree of anaemia and the presence of these intermediate megaloblasts. Some of our patients with haemoglobin levels down to 2 g./100 ml. had only intermediate megaloblasts; others with 6 or more g./100 ml. haemoglobin often have only the typical pernicious anaemia form (Foy *et al.*[9]). Many cases have both the intermediate and the characteristic pernicious anaemia forms, and we have never been able to find any correlation between the degree of anaemia and the presence of these different forms of megaloblasts.

Regarding the relation of the intermediate megaloblasts to iron deficiency, megaloblastic anaemia can, of course, occur in patients who have a concomitant iron deficiency, but it is not our experience that the intermediate form is commoner in patients with such attendant iron deficiency than in patients with characteristic hyperchromic megaloblastic anaemia. In India iron deficiency is very common and megaloblastic anaemia with a concomitant iron deficiency frequent, but the intermediate megaloblast is no commoner in the Indian patients than in the high-altitude African megaloblastic anaemias, where superimposed iron deficiency is far less common. In India megaloblastic anaemia very frequently fails to respond fully to vitamin B_{12} or folic acid unless iron is also given—an indication, we think, that iron deficiency is additionally present. In Africa the majority of the megaloblastic anaemias have high mean corpuscular haemoglobin concentrations and respond to the appropriate haematinic without the addition of iron. Some megaloblastic anaemias have much higher serum vitamin B_{12} levels than others, and, as is well known, this difference is not always correlated with the severity of the anaemia. It may well be that the presence of these intermediate forms is associated with variation in serum vitamin B_{12} levels and not directly with the degree of anaemia.

In Macedonia the majority of the megaloblastic anaemias had a high mean corpuscular haemoglobin concentration, and we rarely saw such an anaemia with a superimposed iron deficiency, yet the intermediate megaloblasts were common. Such anaemias in Macedonia usually responded to vitamin B_{12}; the folic-acid-responding type was rare. From our experience in India, Africa, and Macedonia, it seems that the presence of the intermediate megaloblasts is not directly associated with the degree of anaemia, or related to any concomitant iron deficiency, and that patients with intermediate megaloblasts do not invariably go on to the production of the more characteristic pernicious anaemia megaloblasts.—We are, etc.,

Wellcome Trust Research Laboratories, Nairobi, Kenya. ATHENA KONDI. HENRY FOY.

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Hashimoto's Disease and the L.E. Factor

SIR,—Dr. J. M. Heaton (*Journal*, February 21, p. 466) produced evidence indicating that Sjögren's syndrome is a manifestation of systemic lupus erythematosus. He found L.E. cells in the peripheral blood preparations from 10 of 28 cases of the syndrome. He also noted the similarities between Sjögren's syndrome and Hashimoto's disease and suggested common aetiological factors for both. In an attempt to support this concept, the sera of cases of Hashimoto's disease have been tested for the presence of the L.E. factor.

Method.—Sera (stored frozen at −20° C.) for periods of up to seven months) from 20 cases of Hashimoto's disease were tested by adding to a substrate of fresh leucocytes and serum. Stored sera from two cases of systemic lupus erythematosus were tested as controls. The 20 sera tested were selected by their giving positive thyroid precipitin tests. *Results.*—The L.E. factor was not detected in any one of the 20 sera. The control sera produced L.E. cells.

The absence of the L.E. factor in 20 cases of Hashimoto's disease does not support the suggestion that this disease is a manifestation of systemic lupus erythematosus. We thank Dr. L. Parker for providing the sera from the cases of Hashimoto's disease, which were under the care of Dr. R. W. Luxton.—We are, etc.,

Crumpsall Hospital, Manchester, 8.

E. CHRISTIAN.
D. W. DAWSON.

Acquisition of B-like Antigen

SIR,—The recent reports of A_1 individuals whose red cells react with certain anti-B sera, presumably due to an acquired B, or B-like, antigen, prompt us to report a further case to add to the 11 already described by Dr. C. Cameron *et al.* (*Journal*, July 11, p. 29), Mr. C. M. Giles *et al.* (p. 32), and Mr. W. L. Marsh *et al.* (*Journal*, July 18, p. 63), and to suggest a hypothesis for the origin of the acquired antigen.

Mrs. M. G., aged 75, suffering from carcinoma of the rectum and hypertension, was found group A_1 (β), Le(a-b-), and a secretor of A and H, but not of B; her cells were agglutinated by 11 out of 34 β sera. Four and a half months later her cells reacted as a normal A_1.

We would also like to report that the cells of Mrs. B. L. (Case No. 28, Stratton and Renton[1]) reacted as a normal A_1 when retested 19 months after our original findings. Marsh *et al.* suggest that the altered reactions of the red cells in these cases are due to bacterial enzymes, and it is interesting to note that polyagglutinability of red cells has always been attributed to the same cause (Friedenreich[2]), though it is thought by some that polyagglutinability is due to the adsorption of bacterial polysaccharides on to the red cell surface. The acquired B antigen also resembles polyagglutinability in being a transient phenomenon, and indeed three of the cases showed some degree of polyagglutinability in addition to having a β-specificity.

Neter *et al.*[3] have used red cells coated with bacterial antigens *in vitro* for the detection of antibodies to various salmonellae, and we ourselves found that red cells take up *E. coli* polysaccharide *in vitro* when only a few micrograms are present and are strongly agglutinated by normal human sera. If adsorption of polysaccharide took place *in vivo* in certain circumstances, it is possible that an apparently altered blood group would result. The organism concerned might well be an *E. coli*, since Springer *et al.*[4] have shown that *E. coli* O_{86} polysaccharide possesses strong blood group B activity, and, moreover, when this organism was fed to chicks reared under sterile conditions, a potent anti-B was produced.

It is interesting that all the patients described were group A_1, that all had surgical conditions (two had gangrene of the leg), and that many were old, and the suggestion of Fine *et al.*[5] that traumatic shock is related to the entry of *E. coli* or other bacterial endotoxins from the gastro-intestinal tract appears relevant. Perhaps, also, old age is associated with a diminished antibody response, so that the patient is less able to eliminate the foreign polysaccharide, and perhaps the anti-B of group A_1 individuals is less effective in this respect than that of group O individuals.

This acquired change of blood group may have wider implications, and it is hoped that further cases of this fascinating phenomenon will give an opportunity for testing the hypothesis that this change in the red cells is due to adsorption of polysaccharides of B-like activity.—We are, etc.,

National Blood Transfusion Service, Manchester, 1.

F. STRATTON.
P. H. RENTON.

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Tobacco Amblyopia

SIR,—Permit me to comment briefly on your leading article on tobacco amblyopia (*Journal*, June 20, p. 1582). (1) Tobacco amblyopia never develops from the ingestion of alcohol alone. (2) Cigarette smoking may cause tobacco amblyopia. (3) Tobacco amblyopia is relieved by the exhibition of vitamin B_{12}. Smoking may be continued.

You state that amblyopia may follow the ingestion of alcohol. True: but not tobacco amblyopia, which is a characteristic and distinct entity. Quatermass's case[1] referred to was reported as a case of B_1 deficiency associated with the consumption of large quantities of alcohol. The visual field changes were consistent with this and showed none of the characteristics considered by Duke-Elder[2] or Traquair[3] to be indicative of tobacco amblyopia. It is generally considered that heavy cigarette smoking, inhaling tobacco dust, or chewing tobacco may occasionally cause tobacco amblyopia, in addition to pipe smoking. The main treatment need not now necessarily involve abstinence from tobacco (Duke-Elder[4]; Heaton, McCormick, and Freeman[5]).

The administration of vitamin B_{12} is vastly more effective than that of vitamin B_1 alone, and, indeed, the effectiveness of the latter may be due to the fact that some commercial preparations of B_1 may contain small quantities of B_{12}.[6] It is unfortunate that your leader writer fails to mention a recent and interesting paper.[5] The authors showed that all patients examined with signs of tobacco amblyopia had abnormally low serum B_{12} levels, that tobacco amblyopia may be a manifestation of the "pre-P.A. state" or, more rarely,

of liver dysfunction interfering with B_{12} metabolism, and that treatment with parenteral cyanocobalamin restores the vision, despite continued smoking. Whatever their interpretation might be, the facts are there; your leader writer's ignorance of them is depressing.—I am, etc.,

St. Paul's Eye Hospital, Liverpool, 3. C. C. EWING.

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The Occasional Obstetrician

SIR,—The report of Professor A. M. Claye's lecture (*Journal*, August 1, p. 104) prompted me to calculate the size of list a G.P. would require to attain the 20 cases necessary to raise him from the ranks of "occasional obstetricians." In Professor Claye's home city of Leeds, where, he tells us, 70% of deliveries take place in specialist hospitals, some 4,000 patients would be required. While most other areas are less well endowed with specialist beds, it would appear that were the recommendations of the Cranbrook Committee adopted only those G.P.s with large lists could hope to remain on the obstetric list. It is difficult to see how the standard of domiciliary midwifery would be improved by confining its practice to those with the least time to devote to it.

No doubt one member of a group could undertake to do all the practice obstetrics. Unless he were prepared to take more than his share of night duty, at least half of his patients could expect to be delivered by a partner who (officially at any rate) had given up all interest in obstetrics. As an "occasional obstetrician" who believes that midwifery is as essential to true family practice as it is rewarding I doubt if I would be alone in preferring to continue to work for a woefully inadequate remuneration rather than refer my patients to a neighbouring practitioner.

Surely, in a field where so much depends on painstaking attention to detail and routine, the "occasional obstetrician" is liable to make less mistakes than the "overworked obstetrician."—I am, etc.,

Enfield, Middlesex. J. F. WOOD.

Diagnosing Gall-stones

SIR,—The importance of accurate observation and appreciation of symptoms and physical signs is no better illustrated than in gall-bladder disease, where the family doctor often tells the surgeon that stones are present even when detailed investigation says they are not. Frequently, when the patient reaches the surgeon the attack of gall-stone colic is over and the bladder is not tender to palpation through the anterior abdominal wall. The radiologist may contribute the observation that the gall-bladder does not fill and no radio-opaque stones are present. Cold comfort to a suffering woman.

Twice in the last two years the same general practitioner has said to me in such a case: "I am sure there are stones because I have seen an attack of biliary colic, although there was no jaundice." In both cases, one of whom was his wife, because of my high opinion of this doctor's work I removed a gall-bladder full of stones. The corollary is equally important. The surgeon should be given the opportunity of seeing patients while abdominal pain is present, particularly in suspected gall-bladder disease.—I am, etc.,

London, W.1. W. SKYRME REES.

Lumbar Puncture

SIR,—The letter from Mr. W. C. Spackman in your issue of June 6 (p. 1477) should be of interest to all who use spinal anaesthesia. About twenty-five years ago I got the firm of John Bell and Croyden to make me double needles similar to the one which he describes and which I have used continuously. The outer needle, which I push as far as the epidural space, is size 19½ on the standard wire gauge. The inner needle, which is about half an inch (1.25 cm.) longer, penetrates the dura mater and is size 23 S.W.G. I can confirm Mr. Spackman's observation that with a fine needle the incidence of headache is very low. I have also used a needle which was size 26 S.W.G., but I found that this had so narrow a lumen that it was not easy to be sure that the tip of the needle was in the spinal canal, and I therefore abandoned its use.—I am, etc.,

Dorchester, Dorset. J. K. HASLER.

POINTS FROM LETTERS

Mist. N.H.S. Co.

Mr. F. F. MARCHBANK (Horsham) writes: It is surprising that you did not refer in your comments on the Hinchliffe Report (*Journal*, May 16, p. 1285) to one of the most important sentences in the report. It says, "Sometimes formulation can considerably affect the therapeutic efficacy of a drug." This is the first time any official body, or officially appointed committee, has recognized that two preparations of the "same" drug can differ widely in efficacy. This is the case even in so commonplace a drug as an aspirin tablet. Too much moisture causes the acetylsalicylic acid to hydrolyse. Choice of an unsuitable vehicle may result in a hard tablet which does not disintegrate readily, and may pass through the system undissolved. Complex modern drugs are even more unstable and temperamental, easily inactivated by a variety of conditions, and will give maximum efficacy only if all circumstances are adjusted to optimum.

Musical Hazards

Dr. E. V. BEVAN (Cambridge) writes: I am reminded by your correspondence about musical hazards of a story of the late Professor Collingwood, of St. Mary's Hospital. He said that emphysema was a disease, endemic in Harley Street, caused by the sufferers blowing their own trumpets.

Serum Gonadotrophin in Acne

Dr. J. A. WATSON (Auckland, New Zealand) writes: Before accepting the doctrines in the letter by Dr. G. K. Hargreaves (*Journal*, April 11, p. 974) on the use of "gonadyl" (serum gonadotrophin) in acne by the Skin Department of the Leeds General Infirmary, is it not wise to ponder over the methods used by them to query whether "this relatively expensive form of treatment can be recommended as an addition to time-honoured methods?" The late Dr. A. C. Roxburgh said that a girl could produce a recurrence of acne signs overnight if she ate most of a boxful of chocolates. Examination for statistics on acne on one date do not hold good for recording a result which comes out on another. Previous treatment counts, and so does the ordinary word "fluke" when dummies (and splitting of patients) is allowed; and, after all, a few get better by themselves.

Obituary

GEOFFREY EDEN, M.D., F.R.C.P.

Dr. Geoffrey Eden, honorary consulting physician to the Queen Elizabeth Hospital, Birmingham, died peacefully at his home near Portsmouth on July 26. He was 77 years of age.

Geoffrey Hoffmann (he changed his name to Eden in 1921) was born on March 31, 1882, at Bradford, where his father was a leading citizen, a colonel of volunteers, and a justice of the peace. He was educated at Giggleswick School, Caius College, Cambridge, and St. Thomas's Hospital. A good cricketer, he captained his school and won his cricket colours at Caius College. He also played golf for Cambridge against Oxford from 1902 to 1905, being captain in his last year. Qualifying in 1910, he later obtained the degrees of B.Chir. and M.B., proceeding to the M.D. in 1920. He took the M.R.C.P. in 1914, and was elected F.R.C.P. in 1934. After qualification he held several resident posts at St. Thomas's Hospital, including that of resident assistant physician, and he was joint editor of *St. Thomas's Hospital Reports* from 1912 to 1915. After serving in the first world war as a captain in the R.A.M.C., he was appointed assistant physician at the Queen's Hospital, Birmingham, in 1920, later becoming honorary physician to the hospital and its successor, the United Birmingham Hospitals. He was also honorary physician to the Midland Nerve Hospital, Birmingham. He retired from hospital work in 1947.

Eden's work in Birmingham was unobtrusive, for he was a quiet and rather shy man whose interest lay more in the practice of medicine than in medicine as a career, but he took his turn as honorary secretary of the Midland Medical Society. He leaves a widow and three children.

T. L. H. writes: Eden was an excellent clinical physician, devoted to his work and to his patients. Medicine was his life's work and medicine his chief hobby. Formerly he had been a first-class golfer, and, though he gave up the game completely when he went into consulting practice, he could, nevertheless, on occasion with borrowed clubs give the local professional a good game. He was a man of kindly nature but of considerable reserve, which was probably due to shyness, and he took little part in the local affairs of the profession and medical school. He had a singularly happy home life, and he and his wife, Margaret, were a charming host and hostess. I recall with gratitude many evenings spent in their delightful company.

He retired in 1947 to a country house near Portsmouth, where he hoped to continue, in one form or another, his interests in medicine; but the hope was illusory, and he found solace in his later years in tending his garden with a particular interest in growing the rarer vegetables, which he showed to his visitors with a proper pride.

H. I. C. writes: At St. Thomas's Dr. Geoffrey Eden held the post of resident assistant physician during the middle years of the first world war, when it carried unique responsibility, since not only were the physicians to the hospital much occupied with new commitments at military hospitals but all the house-men were called up for service in the R.A.M.C. The scope of the post was almost crippling in its demands, and during 1915–16 he was in sole resident charge of all the medical beds with one over-age house-physician as his only lieutenant. This took considerable toll of his never very robust health, and when he himself was called up he was ordered away by his medical board for three months' sick leave before being allowed to join the R.A.M.C. as a captain. Characteristically, he took only two weeks of leave and finished out the period of deferment by returning to St. Thomas's until a successor could be found.

Eden was a physician of the old school. He had his training before the rise of the application of science to medicine. Although interested in the growth of scientific medicine he generally preferred to rely on his own observations. He was at his best when clues were few and they had to be carefully weighed and evaluated. His keen observation, wealth of clinical experience, and ability to synthesize a complete picture from meagre signs and symptoms stamped him as a clinician of outstanding merit. He was entirely devoted to his work, finding little time left for other activities outside a very happy home life. A man of great integrity who found it difficult to allow even the slightest compromise when principles were at stake, he could neither endure pompousness or humbug in others nor suffer fools gladly. But there are many who have reason to remember him for his kindness and sympathy, as an inordinately hard-working physician, and as a sound teacher of the art of medicine.

B. H. writes: Dr. Geoffrey Eden will always be associated in my mind with the beginning of my life as a general practitioner in Birmingham. To many of us Midland G.P.s he was much more than a consultant to be called in times of difficulty, he was our friend and wise adviser, and it seemed that no time of the day or night was the wrong one at which to ask his help, given always with courtesy and good humour.

His most outstanding quality as a medical man was his power of diagnosis. When I first knew him there were not the modern ancillary aids, and hospital investigation was feared rather than welcomed by the patient. It was at the bedside that the excellence of his clinical acumen was apparent. He followed this with often brilliantly successful unorthodox treatment: thus, he fed his ulcer patients at a time when starvation was the usual treatment, and before psychiatry was an established specialty he used protein shock therapy with great success. Always he bore in mind human as well as medical needs, and his sympathy and encouragement were given freely both to the patient and to the anxious relatives.

Often after the work together had been done, he would exercise his quite remarkable gift of humorous mimicry and regale us with what were almost in the nature of character sketches of the people and patients he had met. Here in Birmingham we are often reminded of him—not the least by those patients whose good health to-day is in great part due to his skill and wisdom. To Mrs. Eden and his children we offer our most sincere sympathy.

D. R. OWEN, F.R.C.S.Ed., M.R.C.S., L.R.C.P.

Dr. D. R. Owen, a Fellow of the British Medical Association and very well known general practitioner in Chester, where he was an alderman and a former mayor, died there on August 10. He was 67 years of age.

David Richard Owen was born in Liverpool on January 10, 1892, the son of the Reverend T. G. Owen. He was educated at Beaumaris Grammar School; the University College of Wales, Aberystwyth, where he was an exhibitioner and a notable games player (captaining the tennis and winning his colours for football and cricket); Trinity College, Cambridge; and the school of medicine at Liverpool. Qualifying M.R.C.S., L.R.C.P. in 1919, he was awarded the George Henry Lewis studentship in physiology at Cambridge, and in 1921 he was co-author with Dr. E. D. Adrian (now Lord Adrian) of a paper on the electrical response of denervated muscle. Leaving Cambridge to study surgery, he held the Thelwell Thomas fellowship in surgical pathology at the University of Liverpool, and after several resident appointments at the Royal Infirmary and other hospitals in Liverpool, and a period as demonstrator of anatomy at the London School of Medicine for Women, he became surgical tutor, registrar, and assistant pathologist at the Royal Northern Hospital, Liverpool. Admitted F.R.C.S.Ed. in 1925, he was appointed honorary assistant surgeon at the Southport Infirmary.

In 1934 he decided to go into general practice in Chester, where he quickly became prominent in local affairs. Elected a member of the city council in 1937, he was mayor in 1947–8, and was made an alderman at the end of his term of office and a J.P. in 1949. For several years he was also chairman of the Chester Education Committee. Dr. Owen served in the R.A.M.C. (T.A.), holding the rank of captain, but he had to relinquish his commission because of ill health at the end of 1939.

Dr. Owen also took a leading part in the medical life of the city. He first represented his Division at Annual Meetings of the B.M.A. in 1938; and became chairman of the Division in 1942, and president of the Lancashire and Cheshire Branch in 1947. First elected to Council in 1943, he remained a member until his death. Chairman of the Chester local medical committee for 21 years, he was vice-chairman of the executive council from its inception, a member of the Liverpool regional hospital board from 1948–58, and a member of the Chester and District Hospital Management Committee from its inception. For all this untiring and devoted work in the interests of his profession he was elected a Fellow of the British Medical Association in 1958.

Dr. Owen is survived by his widow, to whom we extend our sympathy.

H. L. W. W. writes: When David Owen—"D.R.O." to his friends, and we were many—settled in Chester 25 years ago he was perhaps unfortunate in finding no outlet for his undoubted surgical abilities. The surgical staff of the Chester Royal Infirmary were at that time rather young, and no vacancy was to be expected for a number of years. But the Chester Royal Infirmary's loss was the city of Chester's gain. Finding that the work of a busy general practice was not enough, he turned to local government. His predecessor, Dr. John Welsh, had been a Liberal councillor mayor of Chester, and "D.R.O." followed in that tradition.

Though his health was never good—he was invalided out of the R.A.M.C. in 1939 and underwent a major operation 10 years later—he found time in addition to the work on the city council to be a member of numerous other important bodies. He rendered great services to education as chairman of the city of Chester education committee from 1951–7. As a chairman "D.R.O." was not an autocrat, but he usually managed to keep the discussion to the agenda and always knew more about the business than the rest of us. If all these activities were not enough he served with distinction for many years as a member of the Council of the B.M.A.

I have dealt largely with his outside activities, but there are many people in and around Chester who will always remember Dr. Owen as their family doctor, a wise counsellor, and their friend.

W. W. FRANCIS, M.D.

Dr. W. W. Francis, librarian of the Osler Library at McGill University, died at Montreal on August 10, aged 81.

Sir ARTHUR MACNALTY writes: In the death of Bill Francis I mourn not only a great medical historian and bibliophile but a friend of many years' standing. We lived under the same roof in Bloomsbury when I was a medical student at University College Hospital and he was studying children's diseases at Great Ormond Street Hospital. His mother was Sir William Osler's first cousin, and Osler always spoke of and regarded him as a nephew. He bore a close family resemblance to Sir William in features, in dark eyes flashing with humour, in olive complexion, a heritage of Cornish-Iberian stock, in stature, and in gesture. I was told of a Canadian doctor, Osler's fellow-student, who, meeting Francis for the first time, exclaimed: "It's Osler as a boy again!" Francis had a dreamy air, a friendly smile, and played and sang French songs and Scottish ballads with much charm. Above all he loved books. His knowledge of medical history and bibliophile tastes were a joy to Osler, and they eventually directed his life's work. Francis took me with him on a visit to 13, Norham Gardens, Oxford, and through him my friendship with Sir William and Lady Osler began in my student days.

In 1906 Francis returned to Canada to work in pathology at McGill and to practise as a physician in Montreal. On his visits to England we invariably met either in London or in Oxford. We met once or twice during the first world war; and afterwards he enlisted me as a contributor to the *International Journal of Public Health*, which he successfully edited for nearly two years in Geneva. When this journal ceased publication, he returned to Oxford to undertake his *magnum opus*, the *Bibliotheca Osleriana*, in fulfilment of Osler's last wishes. This will long serve "as an inspiration and guide to the discriminating collector in the whole range of medical history." (Shryock.) When staying with Lady Osler during the years 1922–28, Francis and I spent many hours together in Sir William's library among the books, occupied in tracing references and discussion. After he had departed from Oxford to preside over the Osler Library at McGill with enthusiasm, scholarship, and ability we still kept in touch. In 1939, when I visited Canada on an official mission, I spent a happy week in Montreal seeing Francis, his wife and daughter; Colin Russel, the neurologist; Archibald, the surgeon; and other old friends. Bill and I always wrote to each other several times a year. My last letter from him is dated July 6. It ends, "*Eheu fugaces.* Yes, *omnes eodem cogimur*, but I refuse to address you as *Posthume, Posthume.* You stay put a while."

He was a good classical scholar and could readily quote the Greek and Latin poets. In a letter of December 9, 1951, he writes: "I have just found in the Library the exam. question papers of W.O.'s first (and last) year in Arts, 1868. I no longer imagine I know a little Latin. If he answered a quarter of those Honour Latin and Greek Drama papers they should have elected him president of the Classical Association 50 years earlier than they did." He told me that W. J. Cory took some lines of his poem, *Heraclitus*, from the *Greek Anthology*.

Never robust in health—he had five successive attacks of coronary thrombosis in recent years—Francis's fortitude enabled him to get through an enormous amount of research work and to live to be an octogenarian. He published little in later years, but his well-stored mind was always available to earnest students of medical history, and he helped and guided many to their benefit. He knew his physical limitations, and when McGill offered him a professorial chair he declined it, and, characteristically, never told his family of the offer. Two things greatly pleased him: the volume of tributes from his friends presented to him in 1956 by the Osler Society of McGill University, and the honorary fellowship of the Royal Society of Medicine.

He was happy in his home life, in a devoted wife, in his daughter, Dr. Marian Kelen, in his grandchildren, and in his work. He retained the spirit of youth and laughter to the end. His many friends on both sides of the Atlantic will ever remember him with affection, and will sorrow that they see his face no more.

A. W. F. writes: The news that Billy Francis has died in Montreal will bring tears to many eyes. That he was able to work on in his beloved Osler Library until almost the end will be some consolation. I can so clearly remember his proud joy in Osler's books when I first met him in Oxford in the library of 13, Norham Gardens in 1928, and he was full of the plans for their rehousing at McGill when I had dinner with him in July. During the years between he has been a true friend of the Osler Club of London, helping especially in the preparation for the press of *The Selected Writings of Sir William Osler* published in honour of the centenary of Osler's birth. Oslerians in England have thought gladly of his presence with the books at McGill. His letters and notes, like his conversation, sparkled with his own brand of wit, something bookish

after the style of Dr. James Atkinson, of York, but very human. Those who knew and loved him—and they are many—will share the sorrow of his wife and daughter. But in the years to come, when they turn the pages of the *Bibliotheca Osleriana*, which owes so much to his careful labours, there will be a smile and a twinkle as they remember this whimsical, devoted, and courageous man.

J. G. B. writes: As one of the younger generation of doctors I was wondering if I might be permitted to add a tribute to the late Dr. W. W. Francis? As a junior medical student I had become very interested in Osler through reading *Aequanimitas and Other Addresses*. During that hot summer of 1949 I had a month at the Royal Victoria Hospital, Montreal, and visited the Osler Library, where Dr. Francis himself showed me round and where I was welcome to go at any time. Since then I have had an interest in the history of medicine, the very basis of which is Dr. Francis's catalogue, *Bibliotheca Osleriana*. Though Osler died forty years ago he still is a very real influence among doctors, and by his self-effacing work Dr. Francis must surely rank as one of the chief channels of that influence. A new edition of the quite unobtainable *Bibliotheca Osleriana* would be a most welcome and fitting memorial to Dr. Francis.

H. A. KISCH, M.B., B.S., F.R.C.S.

Mr. Harold Kisch, consulting surgeon to the Royal National Throat, Nose, and Ear Hospital and to the throat, nose, and ear department at University College Hospital, died on July 31, aged 78.

Harold Albert Kisch was born on December 31, 1880, the son of Dr. Albert Kisch. He was educated at the City of London School and St. Thomas's Hospital, qualifying in 1904. Two years later he graduated M.B., B.S., and he took the F.R.C.S. in 1911. At St. Thomas's Kisch was Musgrove scholar, Cheselden medallist, and prizeman in surgery: after qualification he held the appointments of house-surgeon, senior casualty officer, and clinical assistant in the ear department.

After serving throughout the first world war, first with the British Red Cross Society and then in the R.A.M.C., Kisch became assistant surgeon, and soon afterwards surgeon, to the Central London Throat, Nose, and Ear Hospital (now part of the Royal National Throat, Nose, and Ear Hospital). He was also for many years surgeon-in-charge of the nose, throat, and ear department of University College Hospital, surgeon to the nose, throat, and ear department of the London Jewish Hospital, and surgeon to the School for Deaf Children and to the Concert Artistes' Association. For a long period he was dean of the postgraduate medical school attached to the Central London Throat, Nose, and Ear Hospital, which later developed into the Institute of Laryngology and Otology (University of London). A Past-President of the Section of Otology at the Royal Society of Medicine, he also served as vice-president of the Section of Laryngology. His work for the Central London Hospital was perhaps closest to his heart, and he gave devoted service to it for over 40 years.

Kisch had had good experience in general surgery, and he was wont to impress on his students the value of this sound training. A bold and skilful surgeon himself, he welcomed innovations and was ever on the look-out for improved methods. He was a very hard worker, and though his rugged exterior may have seemed to some rather forbidding, he was always prepared to offer his help to his colleagues. Kisch's unfailing cheerfulness, enjoyment of life and human interest particularly endeared him to his junior staff, in spite of his occasional irascibility, when he was apt to express himself with some vehemence. His patients loved him, and his students found him an inspiring teacher and a grand personality.

In 1919 Mr. Kisch married Sybil Hyman, who survives him. There were no children of the marriage.

ELIZABETH C. CLARKE, M.B., B.Ch.

Dr. Elizabeth Clarke died at her home at Maseru, Basutoland, South Africa, on May 17, aged 44.

Elizabeth Chisholm Kirkpatrick was educated at Victoria College, Belfast, and at the Queen's University of Belfast, where she graduated M.B., B.Ch. in 1940. After holding various resident appointments at the Royal Victoria Hospital and the Royal Belfast Hospital for Sick Children, she married Dr. R. E. J. Clarke, and, in 1947, went with him to Basutoland.

J. K. M. and A. J. H. write: Dr. Elizabeth Chisholm Clarke was known to both of us since her student days. Her husband, "Reg," whom she met at Queen's, joined the Colonial Medical Service on his demobilization from the Royal Air Force, and they worked together in the Service in Basutoland until last year, when Elizabeth started in private practice. In her student days she was secretary of the Students' Christian Movement at Queen's for three years and represented Ireland at international conferences, and throughout her life she remained an active, unassuming Christian. Her many interests included the British Red Cross Committee, the United Women's Association, the United Church Committee, and the Victoria League. Elizabeth was respected for her ability as a doctor and she was beloved for her quiet charm, her utter sincerity, and her thoughtfulness for others. Her untimely death is, indeed, deeply felt in Basutoland. Notwithstanding wintry weather, rain and snow, her patients and friends gathered from all parts of the country to pay their last respects at the funeral service. The Government was represented by the resident commissioner and senior officers of the Colonial Service and their wives. The paramount Chief Regent and her retinue were also there, and she wrote later to say that she had lost her best friend. Arriving by car and on foot, more than 600 people, the great majority of whom were Africans, assembled at the graveside. The storm had subsided and the setting sun had come through the clouds as we laid her to rest in a spot surrounded by the snow-capped hills in the land she had served so well. Her memorial is in the hearts of the Basuto people. Our sincere sympathy goes out to her devoted husband, her only son, Robert, and her mother, Mrs. S. Kirkpatrick, now of East London, S. Africa.

JAMES McINTYRE, M.B., Ch.B.

Dr. James McIntyre, who was in general practice in Staffordshire for nearly 30 years, died at his home at Newcastle-under-Lyme on May 26. He was 58 years of age.

James McIntyre was born in Glasgow on April 24, 1901, and was educated at Glasgow University, where he graduated M.B., Ch.B. in 1925. Going first into general practice in Birmingham, he moved to Rugeley in 1929, and then a few years later he went to Burslem. A member of the honorary staff of the North Staffordshire Royal Infirmary for many years, he served as chairman of medical boards under the Ministry of Pensions and National Insurance. He was chairman of the North Staffordshire Division of the British Medical Association in 1944–5, and president of the Staffordshire Branch from 1946 to 1950. He was also a past-president of the North Staffordshire and District Caledonian Society, and a prominent freemason.

J. M. J. writes: "Jimmy" McIntyre was a first-class general practitioner, an excellent obstetrician, and a very good friend. Despite the many offices he had filled, he never could be called an orator. The brevity of his speeches was proverbial, but he did excel as an organizer and as a member of a committee. He was an active member of the executive committee of the North Staffordshire Division of the B.M.A. for over 20 years and of the local medical committee and executive council since their formation, and he seldom missed a meeting. His assessment of any situation was excellent, and there was no one whose advice and criticism I found more helpful. The manner in which he

endured his last illness was typical. Though he knew from the first the inevitable result, he carried on working as long as he was able and never complained, accepting pain and discomfort with stoical courage. Our sympathy goes out to his widow and daughter, to whom he was devoted.

H. E. PEARSE, M.D., F.R.C.S.Ed.

Mr. H. E. Pearse, consultant surgeon at the Musgrove Park branch of the Taunton and Somerset Hospital, died on July 9. He was 55 years of age.

Herbert Edwin Pearse was born on May 22, 1904. After leaving Bristol Grammar School, he entered business, but his interest lay in medicine, and at the age of 25 he became a medical student at Bristol University, where he gained prizes in anatomy and a scholarship in surgery. Qualifying in 1932, he graduated M.B., Ch.B. in 1933, with distinction in anatomy, pathology, and morbid anatomy, and proceeded to the M.D. in 1936. After graduation he was house-surgeon at the Corsham Memorial Hospital, Bristol, and the Royal Free Hospital, London, and senior resident officer at the Taunton and Somerset Hospital before entering general practice in 1935. He still maintained his interest in general surgery, however, and in 1937 he was appointed assistant surgeon at the Taunton and Somerset Hospital, and in 1943 surgeon at the Bridgwater Hospital. He obtained the Fellowship of the Royal College of Surgeons of Edinburgh in 1946, then becoming senior surgeon at the Taunton and Somerset Hospital. He was also consultant surgeon at several other hospitals and to the Somerset police force, and had been director of postgraduate courses in Taunton and had served on the postgraduate educational advisory council of Bristol University.

His interest and experience in surgery, as well as his clinical acumen, made him a successful surgeon, and his opinion, particularly when supported by his experience in general practice, was greatly valued by his colleagues.

K. C. B. writes: Quiet and somewhat modest, Herbert Pearse was a most gentle and charming man who endeared himself to all who knew him, and not least to his patients, who never failed to speak highly of him. His friendships were firm and sincere, and he enjoyed contact with his colleagues, and as a member of the West Somerset Medical Club, of which he was a past-president, he found great happiness and contributed more. For many years, until his work made attendance difficult, he was a member of the Taunton Rotary Club. Although his interests were mainly in his home and family, who gave him so much joy, he took an interest in local affairs and was a member of the local Division of the British Medical Association, and had served on several hospital management and medical committees, to which he contributed much by his sound common sense and quiet, persuasive manner. He will be greatly missed by his colleagues and the staff of the hospitals he served so loyally and well, and indeed by all his many friends, who extend their sincere sympathy to his widow and two daughters in their sad bereavement.

K. R. STOKES, M.R.C.S., L.R.C.P.

Dr. K. R Stokes, medical director of Harefield Hospital, Middlesex, died on July 9.

Kenneth Reginald Stokes was born on January 24, 1901, and studied medicine at St. Bartholomew's Hospital, qualifying M.R.C.S., L.R.C.P. in 1926. Three years later he took up an appointment at Harefield Hospital, when it was a hutted sanatorium. He remained at that hospital for the rest of his life.

L. E. H. writes: Kenneth Stokes became medical director of Harefield Hospital in 1940, at a time when St. Mary's Hospital and Medical School had come into residence. The modern chest and general hospital grew around him and with it his personality expanded, and it was he who absorbed the stresses and growing pains. A man of great sagacity, sound judgment, kindness, and generosity, he made these qualities available to all who were in any kind of difficulty or trouble. It was only necessary to be associated with his beloved Harefield to be assured of his sage counsel and determined support. His chief clinical interest was in the care of the hospital staff, and a large number of nurses owe their rehabilitation and health to his care. His interest in nursing problems was further shown by his honorary secretaryship of the British Tuberculosis Association's nursing committee. In his last public appearance, a few days before his death, he had pleaded for a continuation of facilities for the special training of nurses in tuberculosis. His many friends have the happiest recollections of hours spent in his company in good-humoured philosophical discussion, and of his formidable presence on the cricket field and golf course.

W.S.M. writes: I first met Kenneth Stokes on my arrival as a new boy at Newport intermediate school forty-six years ago. Taking up medicine at about the same time we spent three years together at University College, Cardiff, before proceeding to Bart's. For eight years—until the inevitable scatter that takes place on qualification—we remained the closest of friends. When I returned from abroad in 1948 the old friendship was renewed, and from that date until three weeks before his death I was a frequent visitor to Harefield. Despite the common bond of profession I knew him more as a man than as a doctor. Even as a youngster—rotund of body, with an impish smile on a round face, and the reddest hair I have ever seen—he was a character. Days tramping in the hills above the Usk, rugger excursions up the Welsh valleys, the evening pint of beer after the match, the occasional theatre—he enjoyed them all, and life to the full. As a rugger forward he would work himself to a standstill, a good chap to have on any side. He continued playing until he was 35, after which he concentrated on cricket, playing his Saturday game to the very end. He had a great heart, and was the staunchest of friends. As ready of wit as he was combative in argument, he was very shrewd, with a remarkable human insight and a keen sense of values. Nevertheless, he was very tolerant of the failings of others and generous to a fault. A host of admirers will mourn his loss with the same profound grief and sorrow felt by his more intimate friends.

J. F. McCONCHIE, M.B., Ch.B.

Dr. J. F. McConchie, who was in general practice at Wolsingham, Co. Durham, for over 30 years, died at Newcastle upon Tyne General Hospital on July 10. He was 64 years of age.

James Fleming McConchie was born at Stranraer, Wigtownshire, on April 29, 1895, and was educated at the Royal Academical Institution, Belfast, and at Edinburgh University. At the outbreak of the first world war he volunteered for the Army and joined the King's Own Scottish Borderers, in which he rose to the rank of captain. He left the Army in 1917 to resume his studies and graduated M.B., Ch.B. in 1920. After graduation he held assistantships in general practice at Hebburn, Bristol, and Waltham, near Grimsby.

In 1926 he began practice on his own account in Wolsingham, where he also became factory doctor, Treasury medical officer, and medical officer of the Board of Education and of the Wolsingham steel company. He was also a member of the board of governors of Stanhope Castle approved school. In 1942 he was appointed a justice of the peace, and was chairman of the Wolsingham bench for his last three years. A loyal member of the British Medical Association, he was chairman of the Bishop Auckland Division for one year. For many years he was senior medical officer of Horn Hall Sanatorium, Stanhope, and Leazes Sanatorium, Wolsingham, and under his direction modern equipment for diagnosis and modern antibiotic therapy were introduced.

For the greater part of his time in Wolsingham he was the sole resident practitioner, and his life was a most

exacting one. He was a careful practitioner and spent much time on each patient, never sparing himself. He was regarded with the deepest affection by friends and patients alike, and his presence in the community will long be missed.

Outside his practice and official duties he devoted much time to the affairs of the Wesleyan chapel, of which he was organist and choirmaster. He was a keen gardener, and in his last years had great pleasure in making a beautiful garden around his new house. To his widow and son, Dr. J. L. McConchie, who succeeds him in the practice, we extend our deep sympathy.—J. W. G.

N. A. A. HUGHES, M.R.C.S., L.R.C.P.

Dr. Norman Hughes, who was in general practice at Calverley, near Leeds, for 45 years, died at his home at Menston-in-Wharfedale, on August 2, aged 84.

Norman Alexander Aylmer Hughes was born on July 18, 1875, and was educated at the Yorkshire College, Leeds, the forerunner of the University of Leeds, and qualified M.R.C.S., L.R.C.P. in 1900. Settling in practice at Calverley, he won for himself the love and devotion of the whole community, not only for his professional services, but also for his many interests in the life of the village, which included, in his early days, active participation in local amateur football. He became the true family doctor *par excellence*.

For many years he was medical officer of health for the district, and he was keenly interested in the work of the St. John Ambulance Brigade. During the first world war he served in Malta and France, attaining the rank of major in the R.A.M.C. He was taken prisoner in France in 1918. In the second world war he served on medical boards and in civil defence. On his return from the first world war he became a freemason, and was keenly interested in the craft to the end, holding high office in his lodge. In the service of the B.M.A. he was chairman of the Bradford Division from 1948 to 1950. He had two other enthusiasms to which he was faithful all his life: he was a very active churchman and a great gardener, and from these two sources he derived great pleasure and satisfaction in the years of his retirement. He leaves a widow and two daughters.

LOUISE PEARCE, M.D., Sc.D., LL.D.

Dr. Louise Pearce, formerly a member of the staff of the Rockefeller Institute, died in New York on August 9 at the age of 74. She was closely concerned with the development of tryparsamide as a cure for trypanosomiasis, and was the first to test this drug on human patients.

Louise Pearce was born at Winchester, Mass., on March 4, 1885, and graduated M.D. at Johns Hopkins in 1912. In the following year she joined the staff of the Rockefeller Institute, and remained there until she retired in 1951. At first she worked as Dr. Simon Flexner's assistant, and with Dr. Wade Hampton Brown she investigated the action of arsenic-containing compounds on trypanosomes. Eventually, after successful animal experiments, she went alone to the Belgian Congo to test tryparsamide on human patients suffering from sleeping sickness. Preliminary results were published in the *Journal of Experimental Medicine* in 1921, and her monograph on the subject appeared in 1930.

For many years Dr. Pearce was a notable figure among medical research workers in the U.S.A. She was a member of the National Research Council for a time, and for two years was visiting professor at Peiping Union Medical College in China. In later years she was particularly interested in genetic, physical, and environmental factors in relation to disease. Honoured by the Belgian Government, and by many universities and medical organizations in the U.S.A., Dr. Pearce was a member of the Pathological Society of Great Britain and Ireland and of the Royal Society of Tropical Medicine and Hygiene, and an honorary member of the British Society for the Study of Venereal Diseases.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

In Congregation on May 30 the following degrees were conferred:

M.D.—T. S. Leeson (by proxy), I. B. Smith, R. O. Murray, G. C. Manning.
M.B., B.CHIR.—L. J. Bishop (by proxy).
M.B.—J. M. Stephenson.

UNIVERSITY OF LONDON

The degree of M.D. was awarded to P. W. Darby and J. D. Pollitt on April 20.

The degrees of M.B., B.S. were awarded on May 24 to the following successful candidates:

[1] [6]Ann D. Banister, [1] [3] [4]L. J. Beilin, [1] [2]J. S. Brown, [1] [4] [6]J. S. Cameron, [1] [5]Elizabeth H. Clapham, [1] [2]Sylvia W. Davies, [1] [2] [4]Julia P. Ellis, [1] [4]E. U. Essien, [1] [4]Elizabeth A. Hills, [1] [2]Shirley J. Knight, [1] [2] [6]Jean M. Kubale, [1] [6]M. J. S. Langman, [1] [4]N. J. Legg, [1] [4]R. Marks, [1] [4]R. E. May, [1] [6]T. J. Mott, [1] [4]M. P. Vessey, [1] [4]A. L. Whiteson, S. O. Adenle, Margaret J. Alderton, Jennifer A. Allcock, Abigail E. E. Amua-Sekyi, M. G. Askew, Z. Azari, K. T. Bailey, M. A. McL. Bailey, Katharine E. Barclay, E. J. Barnett, P. R. Barton, G. A. J. Beckley, A. D. Bell, H. C. Bentley, A. Bentovim, A. M. Birt, B. Bisseru, R. Blend, W. F. Bonner, Helen D. Bower, Pearl Bowman, Alice M. Bradley-Moore, J. L. Brady, J. K. Brennand, T. D. Brogan, P. L. Brooks, Dorothy A. Brown, Enid M. Brown, Doreen R. G. Browne, J. C. Bull, A. E. Bullock, D. I. G. Bunn, Jill A. Bunton, R. Burrows-Peakin, Hazel M. Burtenshaw, Christine M. Butler, J. R. Byles, B. G. D. Cameron, Dinan Castle, L. S. Castleden, R. H. C. Catty, P. C. S. Chapman, J. J. S. Chesser, D. D. Chundun, J. H. Cole, Daphne I. Cook, Edith M. Cooke, J. A. Corbett, Catherine M. M. Cordiner, A. M. Cotton, W. M. Cottrell, W. G. R. Couldrick, Felicity C. A. Cox, Jane M. Craig, B. E. Crawley, Barbara A. Croft, D. G. Davies, D. M. Davies, E. T. L. Davies, P. K. B. Davis, P. Dewey, H. Dexter, J. Diamond, G. H. Dickson, Judith Dimock, K. A. Doe, G. Douch, B. L. Dowling, M. S. Duffy, J. T. K. Duncan, C. Dunster, D. J. Y. Dyer, Margaret L. E. Eastcott, Susan C. Estcourt, B. A. Evans, D. S. Evans, Helen C. Evans, H. C. Evans, J. N. G. Evans, Jancis C. Evans-Prosser, Valerie J. Everett, Rosemary Fairweather, Monica J. Falkner, S. E. Farrai, M. A. Farrow, M. A. Fayyad, Elizabeth A. Featherby, L. H. Fenton, P. J. Fenton, Dorothy J. O. ffoulkes-Crabbe, Shirley Fish, A. Franklin, J. J. Franklin, Marie J. Freeman, M. C. Gabriel, Louise Gallagher, G. R. Gerson, A. D. Gibb, D. P. V. L. Giles, T. G. Gilfillan, E. W. Gillison, J. M. Glaisyer, M. Glasser, R. B. Godwin-Austen, Dulcie G. Gooding, P. G. Gooding, A. J. Gould, T. R. Gould, A. E. Green, R. S. Greenwood, Jane M. B. Griffiths, P. R. Grob, A. W. Grogono, D. R. Groves, Anne A. N. Grubb, R. H. Gwyn-Williams, H. Haberfeld, Hanna F. Halaby, Katherine A. Hallidie-Smith, D. Harding-Jones, C. E. Harley, J. A. Harper, J. Harrower, B. A. Hasenson, T. H. Hayle, L. W. H. Hide, B. D. G. Hill, Elizabeth M. Hill, E. J. Holland, J. G. Holmes-Smith, W. Holms, Joan M. Horder, M. Horne, G. I. Horsfield, Judith A. Houghton, J. S. Howard, K. A. Howlett, K. N. Hudson, J. S. M. Hunt, Rosemary A. Hunt, M. F. Hyatt, V. C. Hyman, J. O. Ikpeme, D. C. Jeffery, Ann P. John, W. A. Johns, D. W. McN. Johnson, M. Johnson, T. O. Johnson, A. F. Johnston, B. W. Jones, D. C. Jones, Shirley P. Jones, Y. Joomye, J. M. Justice, A. Kasbarian, J. B. Kelly, M. J. Kettle, R. L. King, F. I. D. Konotey-Ahulu, P. J. Lacey, M. J. F. D. J. Lalouette, Gwenda D. Larkin, C. R. Lattimore, K. D. E. Lawrey, L. A. Lees, O. C. Legg, G. M. Levene, J. H. Lewis, Naomi U. Lewis, Diana J. M. Lister, T. A. Lloyd-James, V. J. E. D. Lobo, Cynthia Lucas, I. S. Macdonald, P. McErlean, Hazel McFarlane, Anne M. Macgregor, C. G. McKenzie, Williamina T. A. McMath, K. S. A. Madgwick, J. J. Maher, Valerie Major, Sheila M. Malcolm, K. J. H. Mallett, K. C. Markwick, Helen K. Marston, J. L. Martin, D. D. Mathews, J. A. Mathias, R. W. May, V. Melikian, D. J. O. Mills, H. J. Missen, J. D. Monger, J. Monro, Margaret J. Moody, M. R. R. Moore, B. D. G. Morgan, Mary J. Morgan, Jean Morris, G. O. Morse, J. M. Motsieloa, J. C. Mountain, D. F. Munt, A. I. S. Murray, Mary A. Murray, Margaret L. Neale, Joan F. Nicholls, J. L. N'mmo, J. E. Noakes, R. G. Notley, E. L. Offerman, Barbara E. P. Ogden, Ruth Ogden, J. W. O'Higgins, E. E. Okafor, A. O. Olowu, D. J. Openshaw, E. H. Osborn-Smith, J. Owens, H. L. Parfitt, Kathleen P. Parfitt, P. G. Parry, Adiline W. Patterson, M. J. Patterson, D. K. Payler, P. E. Pearce, W. B. Pearce, J. G. Pegg, D. G. Pendlebury, Audrey E. Pett, A. D. Piatkus, F. W. Pick, Jean S. Pilkington, A. Plews, R. C. H. Pollard, L. W. Purnell, R. J. Purnell, N. A. Purry, C. A. Ramsay, C. L. Ranasinghe, H. S. Rawdon Smith, D. C. Rawlins, M. I. Reeve, R. W. K. Reeves, P. R. Richards, A. H. Roberts, Jennie Robertson, A. N. M. Robinson, M. D. Robson, P. Robson, B. K. Rogers, W. N. T. Roy, J. J. Russell, M. D. Sanders, M. Sarner, D. A. Scarisbrick, J. G. Sekabunga, Anne Seymour, Margaret L. Shaw, H. D. Sherbourne, M. D. Sidell, P. H. Sills, M. O. Sime, R. B. D. Skidmore, Amy E. T. Smith, P. M. Smith, A. W. Sollom, R. W. Sparrow, A. J. Spicer, R. J. Spitzer, June M. Squire, Neilma J. Staunton, J. F. Steele-Perkins, Daphne J. Stevens, I. H. Stevenson, R. G. Swain, R. M. Swinburne, A. R. Tappin, Ann P. Taylor, G. Taylor, T. C. Taylor, A. J. Thomas, J. V. Thomss, W. K. Thomas, Pamela I. Tinslay, J. M. Tomlinson, Catherine R. Townsend, A. F. Tredre, Janet B. Tyler, M. J. Tyrrell, Joyce C. Vale, A. Vejjajiva, C. D. Walker, J. A. Wall, Rosemary V. H. Ward, Joyce Wardle, Margaret J. Watt, W. F. Webb, G. S. Welch, Mary K. West, Margaret J. Wharton, D. J. White, R. W. White, P. T. Whitehead, M. P. Wilderspin, M. C. T. Wilkes, M. K. Williams, B. C. Williamson, G. T. Wills, C. R. Willson-Pepper, H. S. Winsey, J. Wolffe, M. J. F. Woolmore, D. S. Wright, R. J. Wrighton.

[1]With honours. [2]Distinguished in pathology. [3]Distinguished in medicine. [4]Distinguished in applied pharmacology and therapeutics. [5]Distinguished in surgery. [6]Distunguished in obstetrics and gynaecology.

UNIVERSITY OF LEEDS

The following candidates have been approved at the following examinations:

M.D.—D. A. Cahal (with distinction).
D.P.H.—F. N. Bamford, Gladys V. Bradshaw, J. Ll. Evans, Jamesina Felgate, G. Firth, T. F. McC. Jackson, R. C. Laverick, D. S. Pickup, B. Reffold, D. J. Roberts, C. M. Samuel, Ruth R. Stoakley, Jill C. White.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

The following candidates have been awarded the Diploma in Obstetrics:

P. J. Adams, K. D. Allardyce, C. J. Allen, D. L. Almond, Mary M. Anderson, P. C. W. Anderson, A. Z. Andrzejowski, A. H. Atkinson, A. R. Archer, K. D. Austin, Sheila Bajpai, K. Barker, C. S. Barton, J. R. D. Bedford, N. Beenstock, P. J. Bennison, J. A. Bessell, Anthea Blofeld, A. E. Bloomfield, A. R. Bone, G. A. W. Borland, T. A. Boxall, K. W. Braybou, D. S. C. Brown, E. W. J. Brown, Margaret Brown, J. R. Brunton, A. G. Bryer, J. G. S. Buchanan, Jill M. Buddin, G. D. Burnett, P. J. Burnett, B. H. Burns, Margaret E. Burns, J. L. H. Capper, R. P. Carrington, T. B. Catnach C. Chaurasia, J. H. Chippendale, G. M. Clark, G. A. Clark, Gertrude A. Collie-Kolibabka, Jean R. Colston, S. J. Cooper, W. L. Cordeaux, A. W. M. Core, D. W. Couch, B. S. Cox, F. Cramer, D. Cresswell, J. B. St. C. Cumberbatch, P. Curzen, T. E. Dada, T. C. Dann, D. W. Davies, G. L. Davies, J. F. H. Deeble, B. P. Dillon, K. Dodeja, Margaret E. Dodson, G. V. Donaghy, I. E. Doney, E. M. Douglas, E. V. Dulson, Edna M. Dumbell, Mair A. Edwards, Vivian G. Edwards, D. M. Entwistle, Elizabeth E. Evans, D. A. Ewing, G. R. Fenton, R. S. C. Fergusson, J. W. Fisher, C. V. Foll, R. D. Forbes, W. R. Forbes, J. M. Foster, J. G. Francis, C. R. Frazer, G. B. Gasson, L. J. German, S. D. Giddy, R. A. S. Gilchrist, L. H. Glaser, N. Gorbutt, J. N. Graham-Evans, E. S. Grech, A. J. G. Griffin, M. T. F. Griffiths, G. Gripton, C. Gunn, Cicely R. Haines, J. G. Hall, J. M. Halpe, R. Hannah, A. J. Harbott, J. Hardy, Sylvie M. Harrison, M. W. Haslett, C. N. Haynes, Joyce R. Hayter, M. J. Hill K. L. Hindle, M. N. Hirons, L. J. Hobbs, E. L. Holland, H. J. Houston, J. W. G. Hughes, J. H. C. Hunt, J. W. Hunt, Rosemary J. Huntley, G. D. Hurrell, R. C. Ilbert, P. K. Irani, Hannah E. Jacoby, D. Jarratt, M. C. Johnson, Barbara D. Jones, K. Jones, M. Kennedy, C. W. Kerr, P. N. Kersley, O. J. Kiener, J. I. King, Ma Hla Kyi, K. T. Kywe, D. W. Laurie, M. H. Lawrence, M. M. Lebbe, J. W. S. Lee, J. V. V. Lewis, H. E. Lichtenstein, D. C. Linahan, Christobel H. Lomax, J. E. R. Lorimer, Elizabeth M. McM. Love, E. G. Lucas, W. L. MacIndoe, G. G. McGarry, R. McLean, C. J. Macaulay, J. C. Mackenzie, I. W. Manson, K. H. Marolia, C. D. May, M. J. A. Menage, I. C. Menzies, J. D. Miller, W. R. Moore, R. C. Mulholland, A. P. Murphy, V. Nagpal, D. Y. Nelson, Grace E. Nicholls, A. M. Nisbet, C. H. Nourse, Florence Y. Obadiah, F. T. O'Brien, Antoinette P. B. O'Donnell, B. K. O'Farrell, D. R. J. Parrott, D. W. Patient, Christine Pattie, Ethel Pereira, P. Phellas, D. H. Pickett, F. J. Pickworth, J. S. Raban, J. L. Ramsay, G. A. Reed, J. M. Ritchie, Pamela A. Roberton, E. R. Roberts, J. Roberts, M. R. G. Robinson, L. C. Rose, I. Ross Russell, G. Rowlands, D. K. Roy, C. S. K. Ruck, W. B. Russell, K. Shamba Shetty, J. A. Shanks, M. Silver, M. N. Simmonds, M. W. J. Smith, R. D. Smith, J. G. Spink, G. P. St. C. Starck, R. H. Stearn, Jessie M. Steele, R. G. Strachan C. D. Strang, D. R. M. Stuart, P. E. N. Suter, Seana R. Sutherland, G. B. Sutton, S. G. Sutton, H. M. Swallow, G. R. Swift, J. A. Taaffe, J. F. Taylor, S. A. W. Taylor, A. Ll. Thomas, K. T. Tighe, K. B. Tyrer, Claudine M. Tyson, R. M. Wainwright, A. K. Walker, J. G. Wall, Rosemary Wall, Barbara J. West, J. J. McL. West, M. S. Whitehouse, P. D. Wickenden, June M. Wilby, D. O. Williams, J. H. B. Williams, Meriel Williams, T. M. Winstanley, R. Winstone, J. F. Wood, A. K. Woodward, S. M. Worrall, M. J. Wright.

Medico-Legal

TATTOO REMOVER KIT

[FROM OUR LEGAL CORRESPONDENT]

On May 11, in the Liverpool County Court, Miss Irene Hanneghan, aged 22, was awarded £60 damages against a television engineer who had sold her a tattoo remover kit for 25s. (*News Chronicle*, May 12). Miss Hanneghan, wishing to remove a tattoo mark from her arm, bought a kit which she saw advertised, and as directed made two applications of the fluid supplied. As a result her arm swelled, she went to hospital, she was away from work for some months, and she now has a permanent scar. Analysis showed that the fluid was almost pure (96.7%) glacial acetic acid.

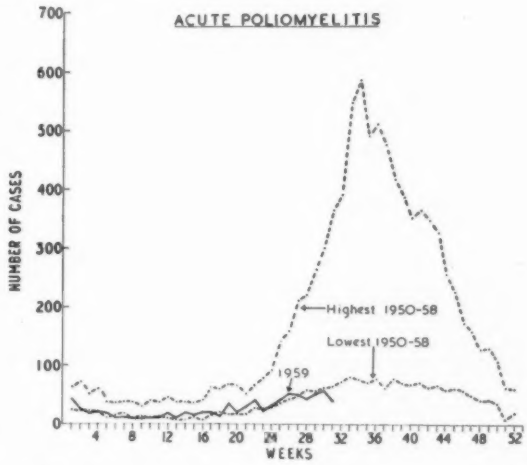
Anyone selling such dangerous substances is liable in respect of any reasonably foreseeable damage, not only to the immediate purchaser but also to any subsequent person to whom the substance is transferred. However, this duty may be discharged if the vendor delivers the article to a person of full age and understanding who either knows of the danger already or is given an adequate warning about it.

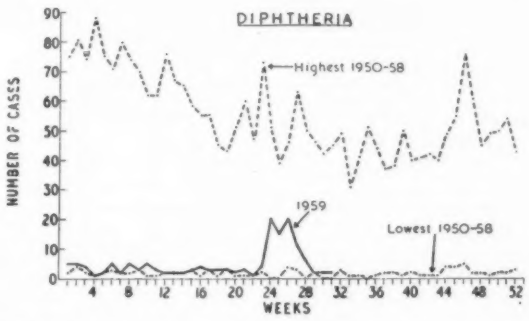
Miss Hanneghan stated to reporters that before buying the tattoo remover kit she had been told at a hospital that she would have to wait two years to have the tattoo removed, owing to the demands of more important cases. If medical practitioners are compelled to postpone treatment in such cases, it would seem most advisable for them to impress on these patients the dangers of self-help, and certainly to urge them to take very seriously any warnings given by manufacturers or vendors.

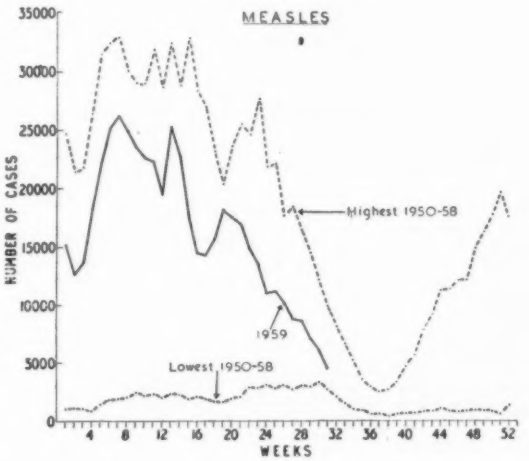
Vital Statistics

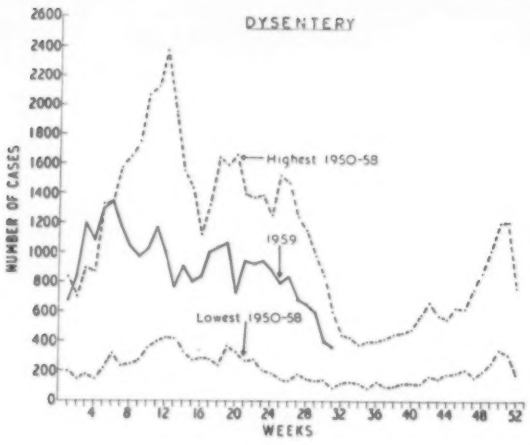
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1950–8 are shown thus - - - - - -, the figures for 1959 thus ———. Except for the curves showing notifications in 1959, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending August 8

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available:

Measles	Week Ending Aug. 1	Week Ending Aug. 8
Gloucestershire	151	**71**
Bristol C.B.	96	**47**
Hampshire	247	**197**
Havant and Waterloo U.D.	100	**62**
Lancashire	613	**517**
Liverpool C.B.	97	**72**
Manchester C.B.	83	**57**
Warwickshire	213	**150**
Birmingham C.B.	119	**75**
Yorkshire West Riding	494	**309**
Sheffield C.B.	108	**57**
Glamorganshire	122	**133**
Port Talbot M.B.	54	**50**
Dysentery		
Lancashire	58	**76**
Liverpool C.B.	16	**19**
Staffordshire	20	**36**
Stafford M.B.	0	**26**
Sussex	14	**13**
Brighton C.B.	14	**10**
Warwickshire	52	**32**
Birmingham C.B.	36	**12**
Yorkshire West Riding	68	**31**
Leeds C.B.	23	**14**
Acute Poliomyelitis		
London	15	**5**
Middlesex	7	**7**
Food Poisoning		
Lancashire	58	**53**
Blackpool C.B.	20	**25**

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in June was 94, compared with 74 in the previous month and 116 in June, 1958.

The numbers of cases of industrial diseases in the United Kingdom reported during June, 1959, were as follows: lead poisoning 3, epitheliomatous ulceration 27, chrome ulceration 12; total 42. There was one death from anthrax, and one from epitheliomatous ulceration due to mineral oil.—*Ministry of Labour Gazette*, July, 1959.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **August 1** (No. 30) and corresponding week 1958.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1959 Eng. & Wales	1959 Lond.	1959 Scot.	1959 N. Ire.	1959 Eire	1958 Eng. & Wales	1958 Lond.	1958 Scot.	1958 N. Ire.	1958 Eire
Diphtheria	6	3		0	1	0	0	2	0	
Dysentery	398	43		23	9	637	118	163	10	1
Encephalitis, acute	6	0		0		5	1		0	
Enteric fever:										
Typhoid	0	0		0	3	0	0	0	0	
Paratyphoid	3	1		0		11	0	4(B)	0	1(B)
Food-poisoning	293	40		3		486	38	23	8	
Infective enteritis or diarrhoea under 2 years				10	43				14	18
Measles*	6,092	133		141	95	6,594	508	39	32	22
Meningococcal infection	13	1		0		16	0	16	1	
Ophthalmia neonatorum	17	3		0	1	15	1	5	0	
Pneumonia†	146	12		7		182	15	107	1	
Poliomyelitis, acute:										
Paralytic	35	6		0		38	2	26	5	10
Non-paralytic	23	9				25	2			
Puerperal fever§	207	33		0		188	25	4	0	
Scarlet fever	627	31		9	20	672	48	28	14	21
Tuberculosis:										
Respiratory	451	74		4		521	59	101	15	
Non-respiratory	64	6		0		73	7	19	7	
Whooping-cough	677	21		35	96	749	37	71	39	58

DEATHS	1959 Eng. & Wales	1959 Lond.	1959 Scot.	1959 N. Ire.	1959 Eire	1958 Eng. & Wales	1958 Lond.	1958 Scot.	1958 N. Ire.	1958 Eire
Diphtheria	0	0		0	0	0	0	0	0	0
Dysentery	1	0		0		0	0		1	
Encephalitis, acute		0			0		0			0
Enteric fever	1	0		0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	2	0		0	0	3	0	0	1	1
Influenza	2	2		0	1	7	1	0	0	0
Measles		0		0	0		0	0	0	
Meningococcal infection		0					0	0		
Pneumonia	298	24		1	6	263	24	9	9	1
Poliomyelitis, acute	4	0		0	0	3	0		0	0
Scarlet fever		0		0	0		0		0	0
Tuberculosis:										
Respiratory	57	6		0	2	59	5	8	0	2
Non-respiratory		0		0	0		3	1	0	0
Whooping-cough	0	0		0	0	0	0	0	0	0
Deaths 0–1 year	266	24	34	13	5	263	25	31	4	3
Deaths (excluding stillbirths)	7,677	572	495	122	119	7,996	597	510	105	137
LIVE BIRTHS	14,687	1256	1061	277	355	13,102	1157	926	197	348
STILLBIRTHS	302	28	17			279	20	19		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Rockefeller Foundation.—During the second quarter of the year the Foundation made grants totalling $8,146,200. The medical and natural sciences absorbed $2,607,499 of this sum. Major grants were provided for the expansion of the Beirut Medical School's research programme, and for the general development of the All-India Institute of Medical Sciences, New Delhi. In this country a two-year $60,000 grant has been made to Birmingham University to purchase research equipment for organic chemistry, and a two-year grant of $28,500 to the Population Investigation Committee, London School of Economics and Political Science, to study changing trends in marriage and divorce in Great Britain and their effect on family life. Research on kuru, a neurological disease occurring in New Guinea, has been furthered by a grant of $10,000 to the University of Adelaide in Australia.

British Association of Urological Surgeons.—The 15th annual meeting of the association, which was a combined meeting with the Canadian Urological Association, was held in Glasgow on July 15 to 18. About 165 members attended, including 21 members of the Canadian association. The main discussion in the scientific programme was on hydronephrosis. The papers will be published in the *British Journal of Urology*. At the annual general meeting the following elections were made for the coming year: President, Mr. DAVID BAND; Immediate Past President, Mr. ARTHUR JACOBS; Vice-president, Professor L. N. PYRAH; Honorary Treasurer, Professor V. W. DIX; Honorary Secretary, Mr. J. D. FERGUSSON; Honorary Editorial Secretary, Mr. N. M. MATHESON; Members of Council: Mr. T. J. MILLIN, Mr. R. A. MOGG, Mr. B. H. PAGE, Mr. D. S. POOLE-WILSON, Mr. F. P. RAPER, Mr. N. L. SHEPPERD, Mr. D. M. WALLACE, Mr. D. INNES WILLIAMS, Mr. W. K. YEATES, and, *ex officio*, the president of the section of urology of the Royal Society of Medicine, and the chairman of the editorial committee of the *British Journal of Urology*.

Royal College of Obstetricians and Gynaecologists.—Council met on July 25 and the present holders of office were re-elected. A new honorary treasurer, Mr. J. H. PEEL, was elected. The following were elected to the membership:

R. M. ADAM, M. A. AUSTIN, P. M. BACON, G. S. BANWELL, A. S. BHANDARY, D. BHATTACHARYYA, S. BISWAS, B. BLOCH, A. A. BOUTWOOD, M. D. CAMERON, A. P. CHAKRAVORTY, S. K. CHAR, D. CHARLES, S. K. CHAUDHURI, E. COOPER, J. D. CROWLEY, I. J. DALRYMPLE, K. DODEJA, D. A. S. EDDIE, E. J. ESLER, J. M. EVANS, W. D. FRASER, S. K. GHAI, J. D. HEHIR, A. HERRIOT, B. J. H. INSULL, C. KATHIRKAMANATHAN, B. G. KOTWANI, T.-H. LEAN, S. LUBERT, R. H. LUMER, K. MCKEE, R. R. MACDONALD, S. K. MANDAL, A. W. MAXWELL, C. D. MOLONEY, K. MUKHERJEE, M. H. MURRAY, K. J. O'CONNOR, C. J. B. ORR, O. M. RAMPERSAUD, J. A. RIEDEL, J. G. ROBERTSON, M. L. ROBINSON, D. W. A. RODWELL, N. N. ROY CHOWDHURY, C. J. RYAN, J. M. SAMSON, S. A. SELIGMAN, N. G. STEERE, D. P. G. STEWART, R. H. SYRED, B. A. TAYLOR, J. H. TAYLOR, G. WADE, P. A. WALKER, J. B. WEDANDE, C. R. WHITFIELD, and A. C. WILSON.

M.R.C.P. (Ed.).—At a quarterly meeting of the College on July 28, the following were elected Members:

E. SAMUEL, J. M. STOWERS, P. DAMODARAM, H. R. OHRI, P. A. DUKE, J. F. CLEOBURY, M. KRISHNASWAMY, P. K. GHOSH, D. J. BREWER, A. M. RAHMAN, R. S. GILL, P. A. ELLIS, K. S. R. BEDI, IHSAN-UL-HAQUE, H. GORDON, H. ISAACS, H. C. B. BARNES, G. B. LANGAN, FAZAL-UR-RAHMAN, J. C. BARUA, S. BARUA, R. H. DAVISON, A. H. MEHAL, T. P. DEVARAJ, P. K. ADHIKARI, G. CLENNAR, E. L. HARRIS, R. HUME, R. T. T. YOUNG, J. S. EAPEN, I. KRUPANIDHI, H. A. MEREDITH, K.-C. TSANG, IKRAM-UL-HAQ, R. P. PILLAY, P. E. B. RODGERS, R. K. S. DHARIWAL, H. L. UTIAN, R. M. MCCREDIE, S. R. KAMAT, M. HAYAT, M. A. ILAHI, D. RABINOWITZ.

Cambridge Chair of Criminology.—The Council of the Senate has recommended the establishment of a Wolfson professorship of criminology from October 1. The first holder of the chair will be Dr. LEON RADZINOWICZ, of Trinity College, the director of the department of criminal science.

Wellcome Foundation Exhibition.—An exhibition of five pharmacies, reconstructed from material collected by the late Sir Henry Wellcome and now owned by the Wellcome Historical Medical Museum, was opened on July 1 by Mr. M. PERRIN, chairman of the Wellcome Foundation Limited. Dr. E. A. UNDERWOOD, director of the Wellcome Historical Medical Museum and Library, also welcomed the guests. The pharmacies include an Arab pharmacy, shops from seventeenth-century England and Italy, a Hispano-Mauresque pharmacy of the late eighteenth century, and John Bell's well-known establishment which did business in Oxford Street until 1909, and is illustrated here. Historical

[By courtesy of the Wellcome Foundation

interest apart, one of the most striking features of the pharmacies is the great beauty of the common objects they contain. The blue-green jars on the shelves of the Arab pharmacy, each slightly different in colour, and affectionately decorated with inky patterns of faces, birds, fishes, or flowers, are only one instance of the vigorous decorative instinct that is so attractively apparent in this exhibition. It will be open indefinitely.

London University.—The following appointments have been made: Mr. R. COCKER: University chair of dental surgery tenable at King's College Hospital Medical School; Dr. F. HOBBIGER: University readership in pharmacology tenable at Middlesex Hospital Medical School; Dr. H. E. DE WARDENER: University readership in medicine tenable at St. Thomas's Hospital Medical School. The title of "Professor of Social Medicine in the University of London" has been conferred on Dr. J. N. MORRIS, in respect of his post at London Hospital Medical College.

Royal Society Research Appointments.—A Locke Research Fellowship has been awarded to Dr. B. G. CRAGG, of the department of anatomy, University College, London, to work there on the connexion and physiological functions of certain nuclei in the brain. Dr. J. S. GILLESPIE, of the department of physiology, the University, Glasgow, has been appointed the first Sophie Fricke Royal Society Research Fellow in the Rockefeller Institute. Dr. Gillespie will be leaving the United Kingdom in September, 1959, to take up his appointment at the Rockefeller Institute in New York, where he will be working on intracellular recording from innervated smooth muscle.

Carlsberg–Wellcome Travelling Research Fellowships.—The Carlsberg Foundation (Copenhagen) and the Wellcome Trust (London) announce a third series of awards of

the Carlsberg-Wellcome Travelling fellowships. The successful candidates for 1959–60 are Mr. M. W. BENTZON (the Statistical Department, State Serum Institute, Copenhagen), who will work with Professor M. S. BARTLETT at Manchester University on the application of modern statistical theory to biological problems; and Mr. J. A. HUNT (the Medical Research Council's Research Unit for Molecular Biology, Cavendish Laboratory, Cambridge). Mr. Hunt will study methods of protein chemistry with Professor M. OTTESEN at the Carlsberg Laboratory, Copenhagen.

Telephone Answering Machine.—A machine which will answer a subscriber's telephone in his absence and tell the caller when or where he should call again is to be introduced by the Post Office, it is hoped in October. This was announced by the Postmaster General, Mr. ERNEST MARPLES, in the House of Commons on July 30. The machine will be connected to the subscriber's telephone line and he will be able to record announcements of about 16 seconds' duration. When the machine is switched on it will play back the announcement to all callers. There will be an installation charge of £2 for the machine at a quarterly rental of £10.

Prize for Clinical Research in General Practice.—Through the generosity of the Sir Halley Stewart Trust, the Society for Psychosomatic Research is offering two prizes of £50 each for a paper reporting original research within general practice on some aspect of psychosomatic medicine. Details from the Secretary, 96, Portland Place, London, W.1.

Blood Transfusion Award.—The Oliver Memorial Fund Committee invites applications on behalf of candidates for the Fund's twelfth annual award of £50. The award is for notable original work or service by a British subject in the research, organizational, or donor fields of blood transfusion. Applications should be made by September 30 to the honorary secretary, Mrs. F. E. BEDBOROUGH, 105, New Park Avenue, London, N.13.

Army Appointments.—Brigadier R. A. STEPHEN, late Royal Army Medical Corps, is to become director of surgery and consulting surgeon to the Army in December; Brigadier W. R. M. DREW, late Royal Army Medical Corps, has been appointed director of medicine and consulting physician to the Army.

Ford Foundation—E.S.U. Travel Grant.—The grant for a doctor in general practice to travel in America has been awarded to Dr. THOMAS GARDNER, of Carlisle.

Br-r-r.—Dr. HIRAM BADDELEY, aged 45, of Uxbridge, his son, aged 21, and his daughter, aged 15, swam the 10½ miles from Lakeside to Waterhead, Lake Windermere, on August 15 in just over 11 hours. Dr. Baddeley said afterwards that he had arranged the swim mainly to study the effects of cold on the human frame.

COMING EVENTS

British Association for the Advancement of Science.—Annual meeting, York, September 2–9. Details from the Secretary, 18, Adam Street, Adelphi, London, W.C.2.

Cambridge University Postgraduate Medical School.—Symposium on "Depression," September 22–26. Details from the Secretary of the School, Tennis Court Road, Cambridge.

International Scientific Film Association.—13th Congress, London and Oxford, September 23–October 2. Details from the association, 3, Belgrave Square, London, S.W.1.

"Some Aspects of Adrenal Deficiency."—An open lecture by Professor A. GORMAN HILLS (University of Miami School of Medicine) in the Courtauld Lecture Theatre, The Middlesex Hospital, London, W.1, on September 3, 5.15 p.m.

Students' International Clinical Conference.—A conference on "Recent Advances in British Medicine" will be held at the University of St. Andrews, Queen's College, Dundee, on September 6 to 19. It is sponsored by the British Medical Students' Association and the International Federation of Medical Students' Association. Details from SYDNEY WAIN, B.M.S.A., Queen's College, Dundee, Scotland.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Thorax.—Issued quarterly (£3 annually). The new issue (Vol. 14, No. 2) includes:

OBSERVATIONS ON THE ELECTROENCEPHALOGRAPH DURING EXPERIMENTAL AND CLINICAL CARDIO-PULMONARY BY-PASS. P. Cliffe, Charles Drew, Gerald Keen, and D. B. Benazon.

THE RADIOLOGICAL AND BACTERIOLOGICAL ASSESSMENT OF TUBERCULOUS LUNG LESIONS REMAINING AFTER CHEMOTHERAPY. A. W. T. Eade, G. Kent Harrison, S. E. Large, J. Mackay-Dick, Lynne Reid, and R. W. Riddell.

PATTERNS OF DISTURBED LUNG FUNCTION IN PATIENTS WITH CHRONIC OBSTRUCTIVE VESICULAR EMPHYSEMA. Colin Ogilvie.

THE EFFECT OF PULMONARY ISCHAEMIA ON LUNG FUNCTION. H. W. Hankinson and F. Ronald Edwards.

THE OESOPHAGO-GASTRIC SPHINCTER AFTER CARDIOMYOTOMY. Michael Atkinson.

FURTHER OBSERVATIONS ON THE GASTRO-OESOPHAGEAL JUNCTION. B. Creamer, G. Kent Harrison, and J. W. Pierce.

THE CONNECTIVE TISSUE SEPTA IN THE ADULT HUMAN LUNG. Lynne Reid.

THE EFFECTS OF BRONCHODILATORS ON PULMONARY VENTILATION AND DIFFUSION IN ASTHMA AND EMPHYSEMA. Gerard Lorriman.

PARTITIONAL RESPIROMETRY IN CARDIO-PULMONARY DISEASE. Roy J. Shephard.

THE FORCED EXPIRATORY VOLUME AFTER EXERCISE, FORCED INSPIRATION, AND THE VALSALVA AND MÜLLER MANŒUVRES. L. H. Capel and J. Smart.

AN ASSESSMENT OF THE STEADY-STATE CARBON MONOXIDE METHOD OF ESTIMATING PULMONARY DIFFUSING CAPACITY. J. MacNamara, F. J. Prime, and J. D. Sinclair.

THE EFFECT OF EXTENSION OF THE HEAD AND NECK UPON THE INFRAHYOID RESPIRATORY PASSAGE AND THE SUPRACLAVICULAR PORTION OF THE HUMAN TRACHEA. R. S. Harris.

INHALED FOREIGN BODIES IN A SERIES OF SUDANESE CASES. W. A. L. MacGowan.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

APPOINTMENTS

DUCAT, E. F., M.B., Ch.B., Clinical Assistant in Paediatrics, Royal United Hospital, Bath.

INSTITUTE OF CHILD HEALTH.—J. A. Black, M.D., M.R.C.P., Senior Lecturer in Child Health, with Consultant Status (from October 1, 1959); J. Lister, M.B., Ch.B., F.R.C.S.Ed., Senior Lecturer in Paediatric Surgery, with Consultant Status (from January 1, 1960).

MANCHESTER REGIONAL HOSPITAL BOARD.—W. K. Douglas, M.B., M.Chir., F.R.C.S., Maximum Part-time Consultant Thoracic Surgeon, South Manchester and West Manchester Groups of Hospitals; P. S. Tweedy, M.D., M.R.C.P., Maximum Part-time Consultant Geriatrician, Stockport and Buxton Group of Hospitals; J. D. P. David, M.D., Whole-time Assistant Physician (S.H.M.O.) in Geriatrics, Bolton and District Hospitals; Lei-Chen Liu, M.D., D.P.M., Whole-time Assistant Psychiatrist (S.H.M.O.), Brockhall Hospital, Langho, near Blackburn; J. C. Denmark, M.B., Ch.B., D.P.M., Whole-time Assistant Psychiatrist (S.H.M.O.), Bolton and District Group of Hospitals.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Leeson.—On August 7, 1959, in Toronto, to Mary (formerly Witcomb.) wife of Dr. T. S. Leeson, a sister for Paul and Gillian.

Pearson.—On July 27, 1959, at New Cross Hospital, Wolverhampton, Staffs, to Jenifer, wife of Noel Pearson, M.B., B.Ch., a second daughter—Anne Margaret.

Wolff.—On August 2, 1959, at the Johns Hopkins Hospital, Baltimore, Maryland, U.S.A., to Catherine, wife of Frederick Wolff, M.D., a sister for Susan and Peter—Catherine Frederica.

DEATHS

Clarke.—On May 17, 1959, at Maseru, Basutoland, South Africa, Elizabeth Chisholm Clarke (formerly Kirkpatrick), M.B., B.Ch.

Croll.—On June 21, 1959, at 33, Albyn Place, Aberdeen, William Flett Croll, M.D.

Darby.—On June 16, 1959, at North Rise, 1, Bredfield Road, Woodbridge, Suffolk, William Sydney Darby, M.B., B.Ch., formerly of Harrow, Middx.

Livingston.—On June 16, 1959, John Livingston, M.D., F.R.C.S.Ed.

Odam.—On June 16, 1959, Charles Leslie Odam, M.R.C.S., L.R.C.P., of 230, Brockley Road, London, S.E., aged 66.

Pardhy.—On June 28, 1959, in hospital, London, Krishna Moreshwar Pardhy, F.R.C.S., formerly of 28, Elvetham Road, Edgbaston, Birmingham, aged 85.

Shipsey.—On June 16, 1959, at his home, 8, Catherine Street, Waterford, Eire, Maurice Shipsey, L.R.C.P.&S.I. and L.M., D.P.H.

Walker.—On June 10, 1959, Robert Septimus Walker, M.R.C.P.Ed., D.P.H., of Courage, Marine Parade East, Lee-on-the-Solent, Hants.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Ether Anaesthesia and Anaphylaxis

Q.—*Does the induction of deep ether anaesthesia before giving tetanus antitoxin intravenously prevent an acute anaphylactic reaction in a patient who is sensitive to horse serum?*

A.—Quill[1] has reported fully a death from anaphylactic shock from tetanus antitoxin given subcutaneously while the patient was under ether anaesthesia and records another anaphylactic shock occurring under ether anaesthesia in a different hospital. Quill reviews the literature, pointing out that while Besredka originated the view that ether anaesthesia protects against anaphylactic shock, numerous other workers have since recorded anaphylactic reactions in sensitized animals under ether anaesthesia and he himself records fatal reactions occurring in 5 out of 5 guinea-pigs, in 5 out of 5 rabbits and in 3 out of 6 dogs, the other 3 dogs having milder but definite anaphylactic reactions. He concludes that ether anaesthesia is valueless as a desensitizing agent and that the practice of administering tetanus antitoxin under ether anaesthesia with the expectation that the anaesthesia will protect the patient should be discontinued.

REFERENCE

[1] Quill, L. M., *J. Amer. med. Ass.*, 1937, **109**, 854.

Oestrous Bleeding and Menstruation

Q.—*Who first discovered that menstruation is not the equivalent of heat in animals?*

A.—It is not possible to say who first "discovered" that menstruation is not the equivalent of heat in animals. The idea gradually developed as a result of the researches of a number of reproductive physiologists, mainly between about 1920 and 1930. From these it became clear that oestrous bleeding occurred at the time of ovulation while menstruation in the menstruating primates occurred some two weeks after ovulation—after progestational development of the endometrium—or, as anovular bleeding, in the absence of evidence of ovulation. Perhaps the observation that most clearly differentiated oestrous bleeding from menstruation was that made by Hartman[1] in the 1930's, to the effect that in rhesus monkeys microscopic evidence of bleeding could be obtained at the time of ovulation—the equivalent of oestrous bleeding—in addition, of course, to menstruation itself. Such mid-cycle bleeding, again mostly microscopic, is also known to occur in some 80% of normal women.

REFERENCE

[1] Hartman, C. G., quoted by Corner, G. W., *The Hormones in Human Reproduction*, 1943. Princeton University Press.

Staphylococci on Theatre Orderlies' Gowns

Q.—*Might operating theatre orderlies moving to and from the theatre about the hospital in their gowns be a factor in the spread of staphylococcal infection?*

A.—In the first place, if the operating theatre is properly ventilated the risk of wound contamination by particles shed from the clothing of occupants not actually alongside the operating table should be small. By proper ventilation is meant a current of clean air descending on the area of the table from above. Secondly, even though the sterile clothing of orderlies may admittedly become contaminated to some extent by these excursions, such contamination is most unlikely to be heavy. A few infected particles might subsequently be liberated, but they would be very few in comparison with the numbers which have recently been shown to be continuously dispersed by skin carriers who are heavy "shedders." On these grounds it seems scarcely worth while to change the present practice, but if it causes anxiety and if an orderly has to go to a considerable distance or to some heavily contaminated environment it should not be impossible for him to remove his gown for the purpose.

Anuria after Concealed Accidental Haemorrhage

Q.—*What is the latest treatment for anuria following a concealed accidental haemorrhage?*

A.—Anuria after concealed accidental haemorrhage is caused by ischaemic kidney lesions of various grades of severity. In some the damage is mainly tubular, in others it involves the entire parenchyme. If bilateral cortical necrosis, the classical complication of abruptio placentae, is so extensive that practically all the cortex is destroyed the patient is doomed irrespective of treatment. If, however, a reasonable number of nephrons are not damaged beyond recovery, or if the lesion is mainly tubular, the patient's life can be saved, so long as she can be kept alive until a measure of renal function returns. In all cases, therefore, the occurrence of anuria demands the immediate institution of a regime designed to keep the blood chemistry compatible with life for as long as possible in the hope that renal function will recover. To this end, the principles independently enunciated by Börst and Bull are still followed, but the method for applying them has changed. Tube feeding, for example, is no longer employed. The main objectives are to avoid overloading the system with fluid and to prevent or limit an electrolyte imbalance. The intake of fluid is therefore restricted to a maximum of 500 ml. in 24 hours (half the volume formerly advised). Many patients, being guided by thirst alone, ask for less than this. The fluid is administered orally in the form of water, weak tea, or coffee (with milk and sugar if desired) and glucose solution. The volume of fluid lost by way of vomit may be replaced, and, when vomiting is persistent, there is sometimes an indication for infusing a concentrated dextrose solution through a polythene catheter into a large vein. All foods containing potassium and protein are avoided so far as possible, so the articles permitted are bread, biscuits, toast, butter, ice-cream, potatoes, rice pudding, and boiled sweets. The patient should be allowed to eat as much of these as she wishes and can even take fats so long as they do not cause vomiting. Meat in any form, meat extracts, fish, fruit, natural fruit juices, and wine are forbidden. By such a diet it is usually possible to keep the patient apparently well (even though the blood urea level may reach 300 to 400 mg. per 100 ml.) despite complete anuria for 14 days and longer.

In the majority of cases of obstetric anuria in which the renal lesion is not irreparable it is unnecessary to resort to treatment by an artificial kidney. If, however, this is contemplated the patient should be moved within reach of the apparatus before her condition is desperate. Changes which might determine a decision to use the artificial kidney include a rise in the serum potassium level to 7 mEq./l., disturbances in the electrocardiograph indicative of myocardial reactions to hyperpotassaemia, acidotic hyperpnoea and drowsiness, and a sustained increase in the blood urea at the rate of 40–50 mg. daily after the first days. A rising serum potassium level can, however, sometimes be checked by enemas of ion-exchange resins, or by the administration of dextrose intravenously and insulin.

Every case of concealed accidental haemorrhage should be regarded as a potential case of anuria. The anuria results from renal ischaemia which is thought to be a reflex response to the uterine condition and to associated shock. The diagnosis of renal failure is at first by no means certain, because shock alone can give rise to temporary oliguria and mild azotaemia. This, however, disappears within 24 hours after delivery, and the persistence of anuria after that time means that some form of renal damage,

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usually cortical, has occurred. In the dramatic case of uterine apoplexy with sudden onset of pain and collapse, the kidneys are likely to be already affected by the time the patient is first seen. In other cases, renal cortical necrosis may possibly be prevented by morphine, by the immediate rupture of the membranes, and by the transfusion of whole blood or packed cells (not blood substitutes) to maintain the level of circulating haemoglobin at a high level. Care should be taken, however, to avoid giving more fluid than is absolutely necessary. At the first examination of the patient the bladder should be emptied by catheter and examined; if any urine obtained is blood-stained there is a high chance of glomerular damage. Thereafter, throughout labour and for the next few days, the intake of fluid and the output of urine should be measured, but catheterization should be avoided lest it lead to pyelonephritis. The specific gravity and urea content of any urine passed should also be estimated because it may represent little more than an insignificant transudate. Until it is reasonably certain that the kidneys are not seriously damaged all protein- and potassium-containing foods should be withheld and the intake of fluid restricted.

Tinned Baby Foods

Q.—*Is the vitamin and mineral content of tinned baby food less than in cooked fresh products?*

A.—The vitamin and mineral content of tinned baby foods is approximately the same as in the fresh products except for two vitamins. Tinned foods in general suffer considerable loss of vitamin B_1 and usually some loss of vitamin C.

Christian-Weber Disease

Q.—*Is there any advance in the treatment of Christian-Weber disease other than steroid therapy?*

A.—No cure for relapsing and febrile nodular non-suppurative panniculitis (Christian-Weber) disease is known, although deep *x*-ray therapy has been claimed to abort these lesions.[1] A number of cases have been recorded which fail to respond to steroid therapy, and, in fact, a nodular panniculitis has been seen to develop as a result of stopping prednisone—usually large doses. Your questioner might consider whether the nodular panniculitis in this case is the reaction to reducing the prednisone used to suppress the previous attack.

REFERENCE

1 Taranta, A., Mark, H., Haas, R. C., and Cooper, N. S., *Amer. J. Med.*, 1958, **25**, 52.

NOTES AND COMMENTS

Dyspareunia after Hysterectomy.—Dr. B. P. BHATTACHARYA (Georgetown, British Guiana) writes: With reference to the answer given in "Any Questions?" (May 23, p. 1360), I beg to mention the following points. (1) Shortening of vagina after vaginal hysterectomy can occur if a lot of vagina is inadvertently removed with the prolapsed cervix. To avoid this, it is preferable to make a racquet-shaped incision of the vagina similar to that used in Fothergill's repair so that the exact portion of the vaginal mucosa to be extracted is marked out. (2) Posterior colpoperineorrhaphy, which is usually the concluding stage in vaginal hysterectomy, helps to increase the length of the vagina rather than shortening it. (3) Dyspareunia following vaginal hysterectomy in addition to short and atrophic vagina (post-menopausal) is mostly due to dryness of the vagina owing to absence of the cervix, whose glandular secretors are the major contribution to vaginal moisture; so it is always advisable to instruct the patient to use some sort of emollient cream during coitus.

OUR EXPERT replies: Of the many factors concerned in dyspareunia after hysterectomy, unnecessarily wide removal of vaginal wall around the cervix was mentioned in the original answer to the question. Dr. Bhattacharya is right to emphasize this, and the incision he suggests is suitable if vaginal hysterectomy is carried out as part of an operation for prolapse. In other circumstances the same objective can be achieved by other techniques. While it is true that posterior colpoperineorrhaphy lengthens the posterior vaginal wall, it does not lengthen the vagina as measured from the lower border of the symphysis pubis to the posterior fornix—the significant measurement so far as coitus is concerned. Moreover, posterior colpoperineorrhaphy only lengthens the posterior wall at the expense of narrowing of the introitus; it should therefore not be practised *routinely* in conjunction with vaginal hysterectomy.[1] Without entering the old argument about the relative importance of cervical mucus, epithelial dissolution, and the secretion of Bartholin's glands in lubricating the vagina between and during coitus, it still has to be recognized that the cervical component of vaginal fluid, being dependent on ovarian activity, virtually disappears after the menopause. The post-menopausal woman therefore lacks this secretion irrespective of whether she is subjected to hysterectomy. The other sources of vaginal fluid also fail after the climacteric, so the ageing woman may well, as Dr. Bhattacharya suggests, find coitus more comfortable if she uses a water-soluble lubricant. Younger women subjected to hysterectomy do not suffer from significant dryness of the vagina during coitus provided that their ovaries are conserved and provided that they retain the libido necessary to activate Bartholin's glands.

REFERENCE

1 Jeffcoate, T. N. A., *Amer. J. Obstet. Gynec.*, 1959, **77**, 490.

Treatment of Tuberculous Cervical Adenitis.—Dr. H. R. E. WALLIS (Bath) writes: Your expert's answer to a question about the treatment of tuberculous cervical adenitis ("Any Questions?" June 6, p. 1488) does not mention the use of calciferol. H. J. Wallace[1] reported favourably on this agent, and S. Gauvain[2] stated: "Calciferol causes an early flare-up of activity, followed generally by rapid healing, which is of such a sound degree that the glands can be immediately and, so far as we can tell at this early stage, safely excised with little risk of recurrence." This was written before the age of chemotherapy; but it seems obvious that calciferol is a very useful adjunct to chemotherapy, and will probably help to save many children from surgery. A suitable dose is 1,000 units per kilogram daily—e.g., for a 7-year-old child 25,000 units and for a 12-year-old 50,000 units daily. I have used similar doses in treating mesenteric adenitis,[3] and no untoward results have been observed. The administration should be continued for four to six weeks.

REFERENCES

1 Wallace, H. J., *Lancet*, 1946, **2**, 88.
2 Gauvain, S., *Tubercle (Lond.)*, 1948, **29**, 259.
3 Wallis, H. R. E., *Brit. med. J.*, 1955, **1**, 128.

OUR EXPERT replies: Dr. Wallis's letter is interesting and confirms, of course, what has been known for some time—that is, that in the absence of other drugs calciferol is useful in the treatment of tuberculous cervical adenitis. However, the modern chemotherapeutic drugs have proved so much more effective that there does not seem any reason for continuing to make use of calciferol. A further reason for being wary of calciferol is the possibility that some renal tubular damage may result in small children treated with a large dosage, although it is true that no gross damage has been reported.

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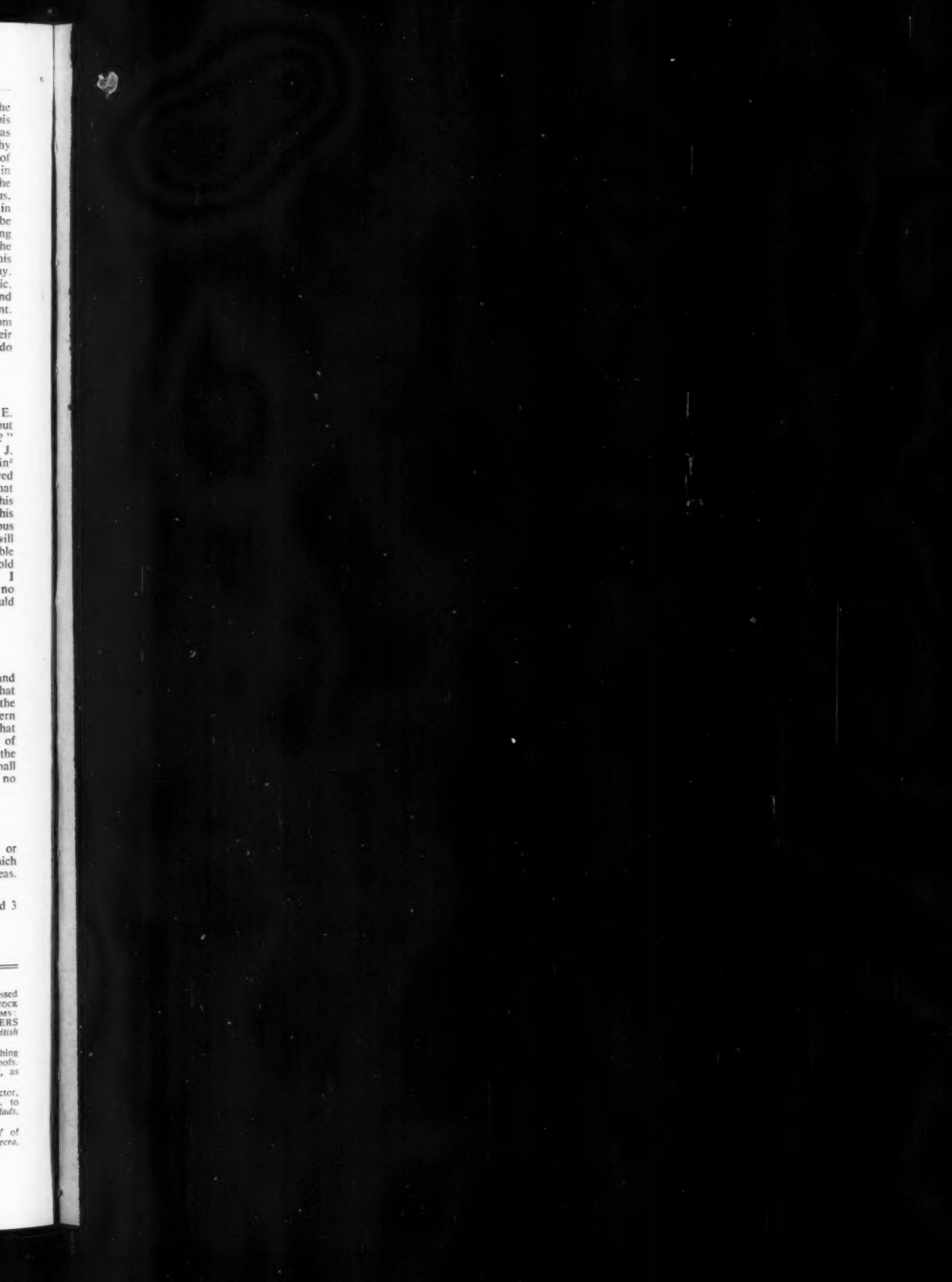
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